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The Betatron[1]

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THIS PAPER IS concerned with a new method for electron acceleration. The principles of the method, which was successfully accomplished for the first time at the University of Illinois (1, 2, 3), will be described briefly, since the type of accelerator used, the betatron, should find worthwhile applications in deep therapy. Some experimental results form the subject of a second paper (p. 120).

In the betatron energy is transferred to electrons by the accelerating effect of a time-varying magnetic field. Since a betatron is a powerful magnet, between the poles of which the electrons circulate in essentially one plane, the apparatus looks somewhat like a small cyclotron. It operates, however, with alternating current instead of direct current, and the process of acceleration is entirely different from that in the cyclotron. The betatron can accelerate particles whose velocity is very close to the velocity of light, such as electrons with energy in excess of half a million volts. Particles accelerated in a cyclotron, on the other hand, must have a velocity much less than that of light, and therefore only heavy positive ions can be accelerated in it to appreciable energies.

Electrons from an electron gun or injector are shot into a circular path within a doughnut-shaped vacuum tube, while the magnetic field intensity is small. As these electrons circulate between the poles of the magnet, the magnetic field is increasing, and the time-rate of change of flux linking the orbit produces an energy gain per revolution equal to that produced by the voltage which would be read on a voltmeter connected to a one-turn coil placed at the orbit and recording instantaneous voltage.

Because of the great number of revolutions described by the electrons while the flux linkage is increasing, the energy in electron volts which is reached is roughly the same as the voltage generated in a secondary coil of the same number of turns placed around the magnetic core of the betatron and acting like a transformer secondary. Thus a betatron is similar to a transformer, but has the advantage that it is unnecessary to produce full voltage on a secondary coil and then apply that voltage to a high-vacuum x-ray tube. The electromotive force is instead continually applied directly to the electron stream.

Figure 1 shows the vacuum "doughnut" in which the electrons circulate many times, having traveled as far as 200 miles when they finally strike the injector, where they produce x-rays and scatter out of the doughnut into the room. The orbit-expanding coils are not energized until after the electrons have been accelerated; they disturb the flux distribution near the

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electron path, causing the electrons to spiral outward until they hit the first obstacle, the injector, which acts as the target. The injection time is indicated at A on the H curve in Fig. 1 (H = the magnetic field), and the orbit is expanded to the target at the time indicated by C, when the energy is at a maximum. These processes are repeated in each cycle with a period of three-fourths of a cycle when no electrons are in the doughnut.

The radius of curvature r of the orbit of an electron of momentum mv is related to the magnetic field causing the circular motion by the equation

$$mv = (e/c)Hr \tag{1}$$

in which e is the electronic charge in e.s.u., c is the speed of light in cm./sec., m is the mass of the electron in grams, v its velocity in cm./sec., and H the magnetic field in oersteds. If r is to be fixed, H must be

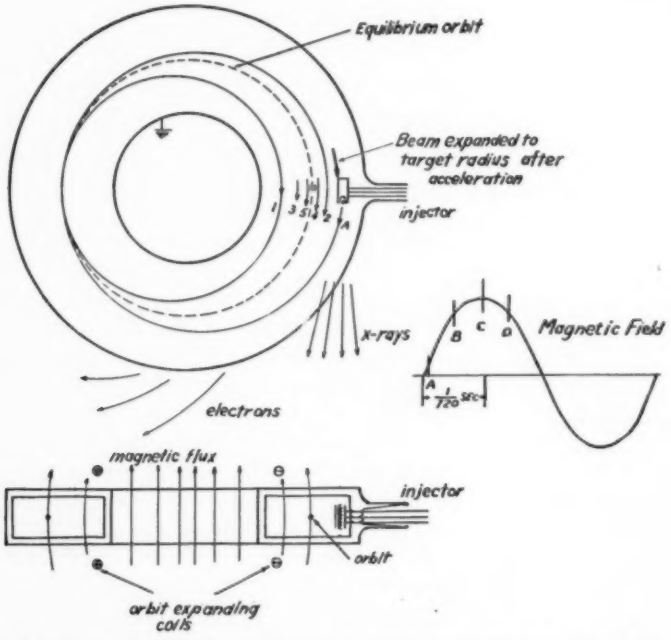

Fig. 1. The doughnut-shaped vacuum tube. Electrons are injected at time A in the magnetic cycle and directed against the target by the orbit expanding coils at time C.

The increase in flux linkage supplies momentum to the electron; and were the magnetic field at the orbit of the electron not increasing simultaneously, the orbit would become larger and larger and soon strike the outer wall of the vacuum chamber. To hold the electron orbit at a fixed radius it is necessary to increase the magnetic field, H, in proportion to the momentum, mv, produced by the increasing flux linkage. This requires a special distribution of magnetic field, as will be shown in the following analysis.

proportional to mv. By Newton's second law the force, f, on an electron is the time-rate of change of momentum, $d(mv)/dt = f$, and this force is the energy gained per unit length of path.

For the present purposes, let us assume that the electron does travel in an orbit of fixed radius; then, since an induced voltage depends on the rate of change of flux linkage, the induced energy gain per centimeter, $f = (e/2\pi rc)d\phi/dt$, where $2\pi r$ is the circumference of the orbit and ϕ is the flux linking the orbit. Integrating

$$mv = \int_0^t f dt = (e/2\pi rc)(\phi - \phi_0) \qquad (2)$$

shows that the momentum is proportional to the change in flux linkage while the electron acquired momentum, mv. Combining (1) and (2) we get

$$\phi - \phi_0 = 2\pi r^2 H \qquad (3)$$

ϕ_0 is the flux linking the orbit when H is zero. This is a very fortunate result since, if both the field at the orbit and the flux within the orbit are produced in the same air gap in the magnetic circuit, ϕ_0 is zero and ϕ is proportional to H. The flux condition (3) is then automatically satisfied.

Although the above analysis has shown that, assuming r_0 is fixed, the flux condition (3) holds, the converse can and must be proved before the design problem can be considered as solved. This was done before the original betatron was constructed, and in the development of the complete theory (3) characteristics of the motion of electrons were discovered which play a vital part in the successful operation of the induction acceleration scheme. It must be possible to form a coherent beam capable of traveling a distance of the order of 100 miles in the vacuum tube without the electrons of the beam straying too far from the equilibrium orbit. A way must also be devised to introduce electrons so that they do not fly out of the acceleration region or hit the starting electrodes after a few revolutions. The theoretical treatment solved these problems.

The stray electrons which are deflected from the equilibrium orbit by scattering from residual gas molecules can be made to oscillate across the equilibrium orbit with a decreasing amplitude so that they eventually are brought back close to the orbit.

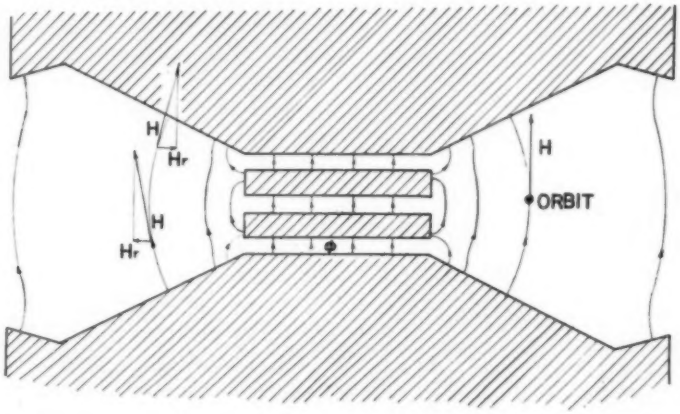

Fig. 2. Curvature of lines of force between the poles of the betatron. There is a radial component to the magnetic field everywhere except in the central plane. The radial component of magnetic field always forces electrons back toward this plane.

By shaping the magnetic field properly, the conditions for this oscillation can be fulfilled. For axial oscillation to occur, the magnetic lines of force must bulge outwardly between the poles, as shown in Figure 2. Then, if an electron deviates from the plane of the equilibrium orbit, it finds itself in a magnetic field with a slight radial component. This radial field is oppositely directed on opposite sides of the plane of the orbit, and it forces the electron, no matter in which direction it is displaced, back toward this plane. This bulging of the magnetic fields is easily accomplished by making the air gap between the poles increase with increasing radius. The pole face looks somewhat conical.

The condition imposed on the shape of the magnetic field for the production of radial oscillations is that the field should not decrease with radius faster than $1/r$. This can be understood by considering the forces required to hold the electron in a circular path and the forces supplied by the magnetic field. Figure 3 shows the

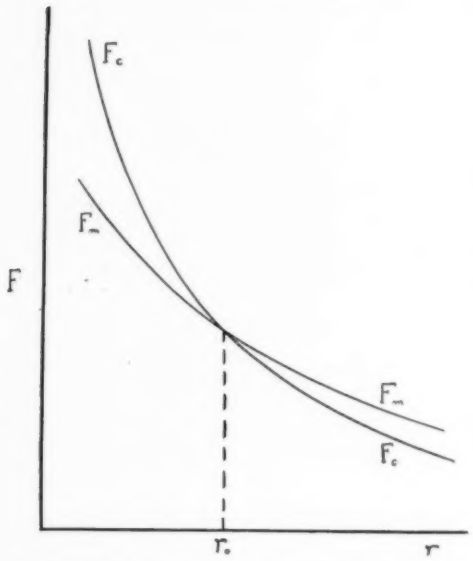

Fig. 3. F_c is the centripetal force mv^2/r required to hold an electron at radius r. $F_m = (e/c)Hr$ is the magnetic force which is supplied to the electron. Radial oscillation occurs about r_0.

force F_c necessary to hold an electron in a circle of radius r. This curve is hyperbolic, since $F = mv^2/r$ and v, the velocity of the electron, is changing so slowly that many focusing oscillations occur before it has altered much. The force, F_m, is the force supplied by the magnetic field. It is $F_m = (e/c)Hv$. If the field, H, is shaped so that F_m is less than F_c when r is less than the radius at the equilibrium orbit, then the magnetic force is not sufficient to hold the electron in at such a small radius. The electron thus will move toward the equilibrium orbit at r_0. If, at radii greater than r_0, F_m is greater than F_c, the magnetic force is more than that necessary to hold the electron in a circle, and the path curves in toward the equilibrium orbit. This shape of field is shown in Figure 3. Thus the stray electron will oscillate about r_0 and also across the plane of the orbit. Both of these oscillations are damped, that is, they have decreasing amplitudes. This is a result of the increasing strength of the magnetic field as time goes on; the amplitude is proportional to $1/H^{1/4}$. The effect of the increasing magnetic field is somewhat analogous to that of a stiffening spring which supports an oscillating mass.

It is because the oscillation of an electron is damped with a relatively large damping when H is small that electrons can be injected from a point at a radius slightly greater or smaller than r_0 and not hit the injector again on one of the first few revolutions. This makes possible the process which is used to get the electrons started.

In the original betatron this damping was made large by operating the magnet at a frequency high for such large flux densities in iron. Six hundred cycles per second alternating current were used, and it was estimated that the time average current striking the target was about 0.03 microamperes. In spite of the small magnitude of the current, the x-ray output in the beam was equivalent to that from about one gram of radium. At the energy which this betatron produced, 2.3 million volts, the x-rays tend to go forward in the direction which the electrons had when they struck the target. This simplifies protection of the operator.

The apparatus used to obtain the 20-million-volt results to be described in the following paper was constructed during a leave of absence from the University at the General Electric Company. It was an intermediate step toward construction following the university's 100-million-volt design. The 20-million-volt betatron (4), now in use at the University of Illinois, operates at a frequency of 180 cycles per second, and it is estimated that the average current reaching the target can be as high as one microampere. An output as great as 50 r/min. in a thick-walled ionization chamber at 70 cm. has been produced at

the maximum energy. The x-rays go forward in a beam which is very pronounced. Although the output voltage of this betatron is less than ten times greater than the voltage of the small betatron, its weight, 3.5 tons, is about 35 times greater than the weight of the original.

While there was no thought that a 100-million-volt betatron could be useful in therapy, as a 20- to 30-million-volt model may prove to be, it was clear from the first operation of the original betatron, that we could plan to use this type of accelerator for certain cosmic ray work in our laboratory. In the design for the 100-million-volt betatron, that was intended for construction on the university campus, I have attempted to save space and materials by using proportions which are not the same as those chosen for the 20-million-volt betatron. There is a smaller fraction of the pole face used for focusing and a larger fraction used for acceleration or increasing flux linkage. While the 20-million-volt betatron gives 1 million volts per inch of pole diameter, the large accelerator is designed for 3/4 inch per million volts. Power and heating problems were also simplified by designing for a 60 cycles per second frequency, which results in a 24,000 kva. unit.

The name betatron, which is now in general usage among physicists, was chosen for the magnetic induction accelerator since it seems likely that the most useful applications of the betatron will involve the production of high-speed electrons or beta rays, as they are known in nuclear physics. When the Greek suffix, tron, is attached to the word beta, the name means the agency for producing high-energy electrons.

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Experimental Depth Dose for 5, 10, 15 and 20-Million-Volt X-Rays[1]

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WITH THE 20-MILLION-volt electron beam of good intensity now produced in the University of Illinois betatron, questions about the practical use of high-energy radiations can be examined. The most promising way to use the betatron in therapy would be to send the original electrons accelerated in the vacuum tube directly into the patient. At 20 million volts these electrons will penetrate as far as 10 cm. and no farther. Thus no damage is done to the back of the patient. Furthermore, the ionization should reach a maximum 7 or 8 cm. beyond the entrance surface for the electrons, and the damage could be well localized within the body. About a 25- or 30-million-volt betatron would be ideal for this work, since it has the right energy and a reasonable size. Although a sufficiently intense beam of electrons now comes out of the betatron, it is not yet in a good enough state of collimation or control for practical use.

The x-rays produced by this electron stream when it strikes a target cause an ionization intensity about as great as that used in practical therapy, while the distribution of ionization in thick sections of tissue-like material shows features very advantageous for deep therapy. The chief characteristics of the high-energy depth-dose curves are: (1) that the point of maximum dose is as deep as 3 or 4 centimeters below the surface of the phantom; (2) this maximum can be several times greater than the surface dose. X-rays in this energy range, therefore, will pass not only through the skin but also through the fat layer under the skin without producing much damage, while the tissue deeper in the body and near the point of maximum ionization will receive a large dose. The desired region in the patient can be placed near the point of maximum ionization intensity, if necessary by compression of his body, and cross-fire will be less important.

In this discussion only experimental results with x-rays and their explanation are presented. Suggestions about dosage measurement, which must be well understood, are also given, since these high-energy radiations have properties which do not show up at lower energies.

For an understanding of the behavior of x-rays of ordinary therapy voltages and also of betatron voltages it is necessary to consider only the Compton absorption process, since it is predominantly responsible for the interaction between these x-rays and tissue-like material. The absorption of an x-ray quantum will produce a secondary Compton electron and a secondary x-ray quantum in all cases.

At low voltages, such as 400 kilovolts, the ionization appears very close to the point where the Compton process occurs, since the resulting electron has only about a 1-millimeter range. The shape of the depth-dose curve is not influenced by the electron range, since it is short. The number of x-ray quanta present at different depths therefore determines the shape of the depth-dose curves, and the low-voltage analysis is based on this fact. In this analysis, the total ionization effect is broken down into two parts: (*a*) the ionization due to the absorption of primary quanta; (*b*) the ionization due to the absorption of secondary quanta (1).

In Figure 1, curve A represents the depth dose observed at 400 kilovolts with the same phantom and ionization chamber which were used at 20 million electron volts. A 400-kilovolt therapy unit at the University of Illinois College of Medicine

[1] Read before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Nov. 30–Dec. 4, 1942.

was used in this work. The components of this curve are B, the ionization due to primary quanta, which falls off approximately exponentially, and C, the ionization due to secondary quanta which are produced at the expense of the primaries, which rises to a maximum and then decreases when more secondaries are absorbed than are produced. This theory for the composition of the depth-dose curve fits the data well in the low-voltage region up to 1 million where it has been tested.

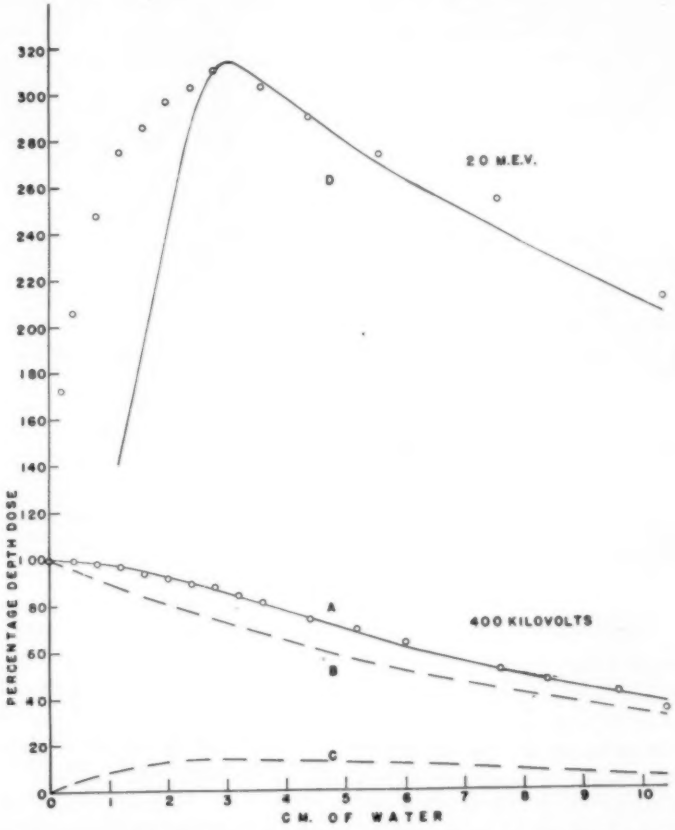

Fig. 1. A. Observed depth dose at 400 kv.p. with 1.15 mm. Sn, 0.25 mm. Cu, 1.0 mm. Al filter, and a 9 × 9-cm. field. B. Primary ionization. C. Ionization due to secondary quanta. D. Distribution of ionization at 20 million electron volts. Points are experimental; solid curve is the theoretical fit.

Two differences in the behavior of radiation at energies as high as 20 million electron volts are responsible for the change in the distribution of ionization produced (Curve D, Fig. 1). First, the secondary quanta curve, corresponding to C, has a very broad maximum at so great a depth that it may be behind the phantom because of the great penetrability. This curve is not shown. Second, the electrons produced in the Compton absorption process may have a range as great as 10 cm. in tissue, and the assumption that the ionization is produced at the location of the Compton process is no longer valid. This second effect is responsible for the large rise to a maximum ionization well below the surface of the phantom. Since the high-energy Compton electrons go approximately forward, the electrons crossing a given plane beneath the surface are mainly those produced in all the material between

the surface and the plane. The number of these electrons increases with the depth, *i.e.*, with the amount of material (between this plane and the surface) which is responsible for the production of the secondary electrons. Not until depths so great that a large fraction of the electrons produced in the surface layer have been stopped does the ionization begin to decrease. The height of the resulting maximum of ionization is also somewhat enhanced by the increasing ionization near the middle of the path of the secondary electrons.

section of the phantom could be placed at any desired depth. Figure 2 shows the ionization chamber. The grounded plate was a 0.005-inch aluminum foil stretched over lucite. Two millimeters behind this was a circular copper plate, which could be charged through an adapter by means of the Victoreen electroscope. Since the secondary electrons causing the ionization can easily penetrate the aluminum sheet, the amount of discharge gave an indication of the ionization at a well defined position in the phantom. The variable separation of the plates in the chamber afforded a

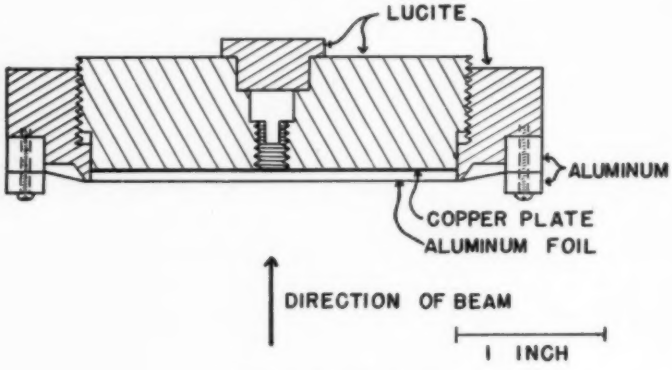

Fig. 2. Ionization chamber.

APPARATUS

The x-ray beam from the betatron, described in the preceding paper (see also reference 2), is well confined in a cone about the direction in which the electrons travel when they strike the target. This cone is capable of covering a field 10 × 10 cm. at a phantom distance of 70 cm. from a semi-thick tungsten target. X-ray intensities as high as 50 r per minute at 70 cm. have been measured in a thick-walled chamber. Depth-dose measurements of the ionization were made in a pressdwood phantom. Twenty-six 1/4-inch sheets of pressdwood formed a phantom 40 × 40 × 16.5 cm. For measurements near the surface, where the ionization rises rapidly, a 1/8-inch sheet was used.

The ionization chamber was fitted into a hole in four sheets of pressdwood. This convenient means for adjusting capacitances. Not shown in the figure is an aquadag coat establishing ground potential on all exterior lucite surfaces. Figure 3 shows the phantom in position in front of the betatron.

EXPERIMENTAL RESULTS

The depth-dose curves (Fig. 4) were taken with x-ray energies of 5, 10, 15, and 20 million electron volts. Since the density of the pressdwood used was 0.65 gm./c.c., all experimental results were converted to water equivalent. Allowance was made not only for the difference in density of pressdwood and water but also for the 5 per cent smaller range of electrons in water than in pressdwood of the same density. The equivalent water phantom has a 45-cm. target-to-surface distance.

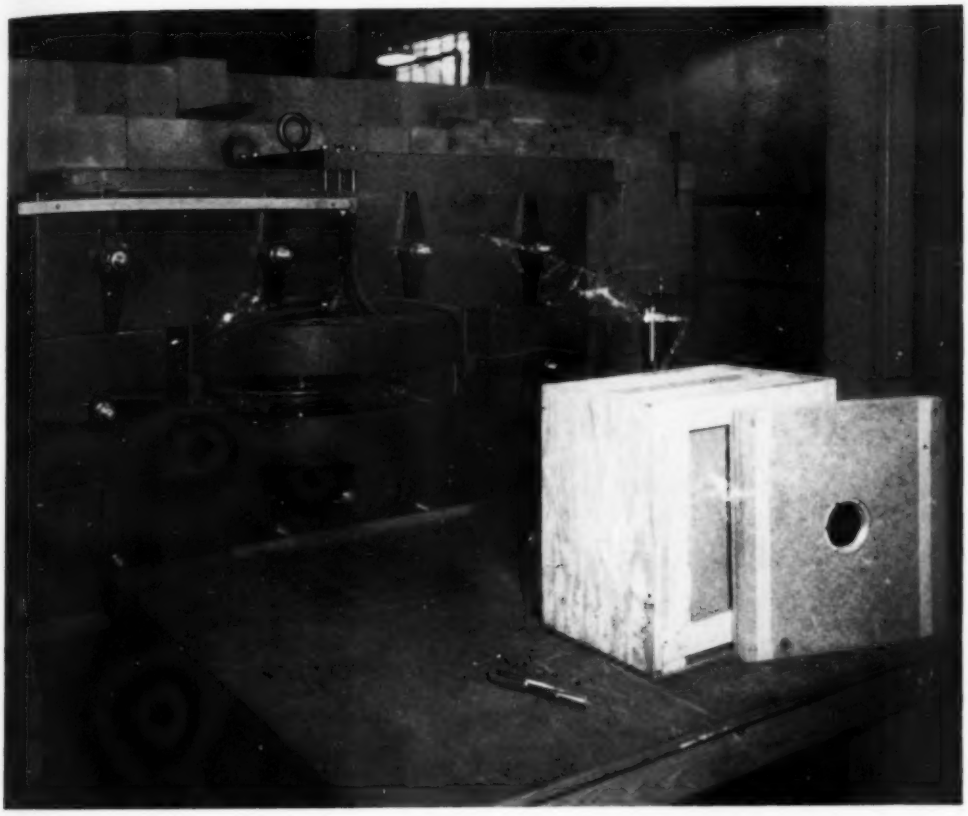

Fig. 3. Phantom in position in front of the betatron.

In low-voltage therapy depth-dose curves are given as per cent of surface dose, since the surface is the point of maximum ionization. At the voltage used in these experiments, however, the maximum is well below the surface of the phantom. The data have therefore been replotted in Figure 5 in a more useful form, as per cent of peak ionization. One of the important features of these high-energy radiations shown here is that the point of maximum ionization moves into the phantom with increasing energy and that the maximum becomes broader. This trend fits in well with the results found by Trump (3) in the range below 4 million volts.

The per cent of peak dose found at 10 cm. is shown in Figure 6. A dose as high as 75 per cent is found at 20 million volts with the target-to-surface distance only 45 centimeters. With the skin-target distance increased to 70 centimeters this dose would be higher.

THEORY

A practical theory of the depth dose may be made for these energies by a simple extension of the method used at energies below 1 Mev (1). Just as at the lower energies (4), measurement of the ionization against depth with a very small field (about 1 sq. cm.), obtained by collimation with pierced heavy lead blocks, showed a nearly exponential fall, when corrected for the inverse square effect. For a 14-Mev electron beam, the absorption coefficient of the x-rays produced was that of a 7-Mev gamma-ray. The theory is based on this fact: that the inhomogeneous primary x-ray beam is absorbed as though it were a

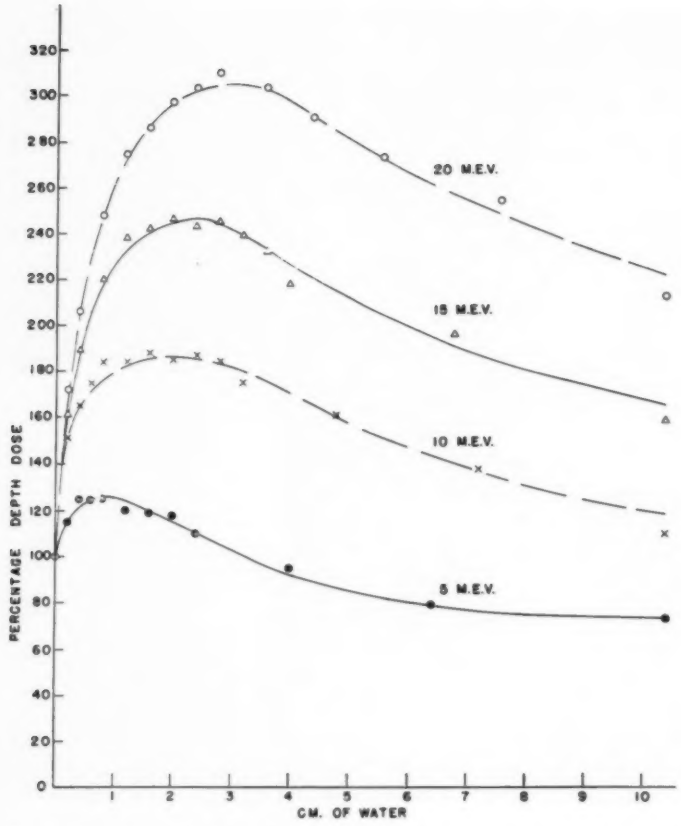

Fig. 4. Experimental results referred to surface dose. Target-to-surface distance 45 cm.

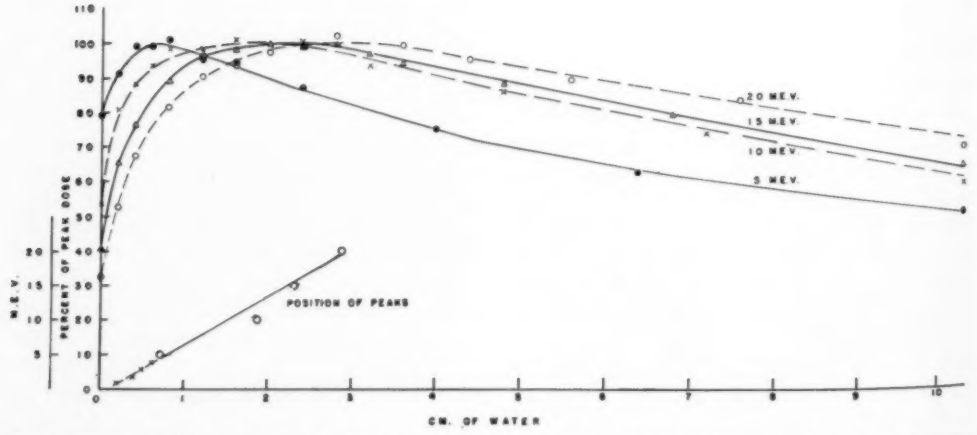

Fig. 5. Top curves show per cent of peak dose. The bottom curve shows the positions of peaks. Crosses indicate Trump's data.

monochromatic x-ray of about half the maximum energy.

When the field is large, secondary radiation also contributes to the ionization. In notation like that of reference 2, the ratio of secondary ionization to initial intensity is

$$I_2/I_0 = f_{2e} f_2 \mu_1 (e^{-\mu_1 x} e^{-\mu_1 x})/(\mu_1 - \mu_2)$$

Here f_{2e} is the number of electrons produced per secondary quantum, f_2 is the number of secondary quanta per primary quantum absorbed, and μ_1, μ_2 are absorption coefficients for primary and secondary quanta, respectively. Near the surface, secondaries are unimportant, but the ionization rises because the electrons contribute over their entire range. In this region, with the same notation, $I_1/I_0 = f_e(1 - e^{-\mu x})$ up to a depth r, the range of the Compton electrons. The primary beyond this depth is proportional to $e^{-\mu x}$. The constant is determined by fitting at the depth r, because the ionization is, of course, continuous. The effective electron range, r, is 3.5 cm. at 10 Mev.

These formulae imply that the ionization produced by an electron is constant until the end of its range. For electrons around 10 Mev, the ionization actually builds up rapidly through about half the range, then falls more slowly. A crude way to include this effect is to represent the ionization as constant for two-thirds of the range, then constant but only two-thirds as great until the end. This was done in the plotted curve.

It is not consistent to attempt a better treatment of the electron-range effect because this non-uniform ionization is chiefly the result of multiple scattering, which causes the electron path to be a very tortuous one—not even approximately straight—complete statistical discussion of which has not been given. Nor are the electrons produced moving in a parallel beam. Also, the effect of the soft component of the x-ray beam will be greatest in these surface layers, as a comparison of the curve and points in Figure 1 will show.

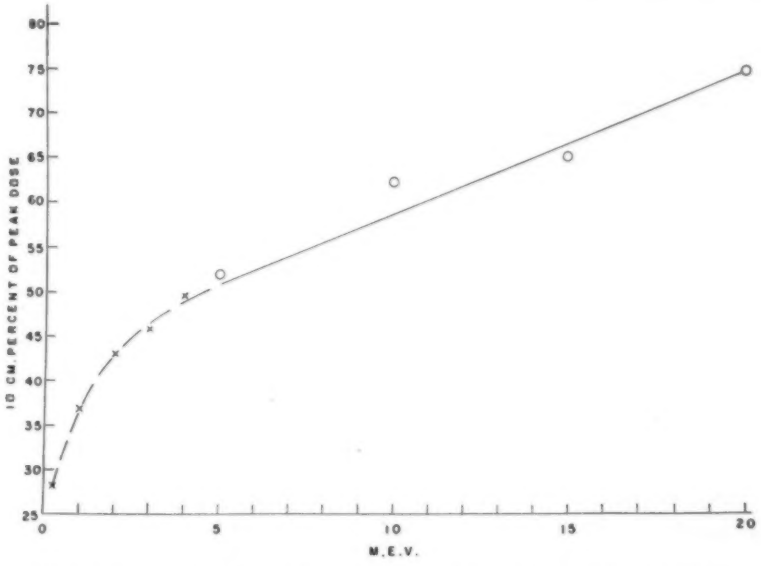

Fig. 6. Per cent of peak dose found at 10 cm. Crosses indicate Trump's data.

DISCUSSION

Experience in taking these data has shown that the surface dose can be greatly affected by stray electrons striking the phantom. These electrons arise from two

sources; some are original beam electrons which escape in large numbers from the acceleration chamber and others are Compton electrons scattered from objects near the x-ray beam. To obtain consistent results the primary electrons were stopped by absorbers placed close to the target, and the secondaries were avoided by keeping scattering objects from the vicinity of the beam. The magnetic field of the betatron undoubtedly removes a great number of secondary electrons. The fact that the per cent of peak dose found at the surface depends critically on the success in eliminating stray electrons indicates that it is dangerous to estimate depth doses from measurements of the surface ionization. A safe procedure for determining absolute dosages is to surround the thimble meter with a thick wall of material equivalent to 10 cm. of water. Dosages occurring at other depths could then be obtained by referring to Figure 5.

With the short skin-target distances used in these experiments, the exit surface dose is kept down to a value comparable with the entrance surface dose. The inverse-square law must be relied upon to reduce this exit dose. Since 45 cm. is about as close to the target of a 20-million-volt betatron as a phantom can be placed, higher energies and larger apparatus make it more difficult to depress the exit dose.

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DISCUSSION

Kenneth Corrigan, Ph.D. (Detroit, Michigan): One thing that Professor Kerst has brought out very well is that the betatron is not a sudden inspiration. The fact is that many people theorized vaguely about the acceleration of electrons by magnetic induction for some years before this development was started. It remained for Professor Kerst to refine the vague thoughts to a precise scientific theory, which he did by working out the equations of his process. He then had both the imagination and the perseverance to see the theory through into substance.

Concerning the measurement on the beam from the betatron, I would like to ask why a copper plate was used in the ionization chamber and just how this plate may have affected the measurements. It is obvious that at the voltages involved in this presentation, the absorption coefficient for copper cannot differ appreciably from that for lighter elements, but since the rest of us have not had the opportunity to make measurements at these voltages, a more exact statement would be of interest.

Also, we should like to hear a word about the problem of protection. Approximately how much protective material is needed, and what kind is best?

It is rare indeed for any society to hear a paper in which everything from the inception of the idea through the development and on finally to such routine considerations as depth dose measurements is presented at once. Professor Kerst's will probably prove to be the year's outstanding contribution.

Helen B. Flynn. M.D. (Chicago, Ill.): It was stated that both electrons and x-rays emerge from the betatron. Is there any way to determine whether the electrons are positively or negatively charged after they leave the machine?

Milton Friedman, M.D. (New York, N. Y.): In his discussion Professor Kerst mentioned the fact that there should be a peak of ionization at a depth of 7 or 8 cm., but in a subsequent curve a peak was shown at about 3.5 or 4 cm. Could he clarify this point?

Leonidas Marinelli, M.A. (New York, N. Y.): I should like to know how large fields could be covered practically with a betatron at the present moment with a certain degree of uniformity—say, within 25 per cent from the edge to the center.

D. W. Kerst, Ph.D. (*closing*): In answering Dr. Corrigan's question about the use of copper as the back plate in the ionization chamber, I can say that it was a thin plate about 0.015 inch thick and that it probably would cut out only a very small fraction of the back-scattered radiation. We have tested back-scattering and have found that at 20 million volts it is of the order of 10 to 13 per cent. There would probably be a slight increase in the sensitivity of the ionization chamber produced by the multiple scattering of electrons in this sheet of copper. Such an effect has been observed in other circumstances.

The x-ray protection about which Dr. Corrigan asked is obtained mainly by staying out of the beam from the betatron. The control panel is situated about 20 feet toward the side and back of the x-ray machine. A two-foot concrete block wall shields

most of the laboratory behind the betatron from the electrons which come out in all directions from the doughnut and from the small intensity of x-rays which come out of the back of the machine. The rest of the room and the control stand are shielded by an additional two feet of concrete blocks, and the x-ray intensity in a region of the laboratory near the control stand is only two to four times as large as the ordinary cosmic ray intensity to which we are continually exposed.

Dr. Flynn asked about the sign of charge on the electrons which emerge from the betatron. Most of them are negative electrons, since their paths are bent in the proper direction by the fringing magnetic field about the magnet; but some positive electrons are undoubtedly created at the x-ray target.

Dr. Friedman's question about the position of the peaks of ionization can be cleared up by restating what the peaks were. The experimental curves shown were obtained with x-rays which penetrated the phantom, and a maximum ionization was created about 3.5 to 4 cm. below the surface when the betatron was operating at 20 million volts. The other ionization distribution referred to in the discussion is that which is expected to occur when the original electrons from the betatron are sent into a phantom. According to Dr. Morrison's estimates, the ionization distribution should rise to a maximum at about 7 or 8 cm. below the surface due to the multiple scattering of electrons, and then it would fall to zero at the extreme range of the electrons, which is 10 cm. for 20-million-volt electrons.

The size of the field, which Dr. Marinelli would like discussed, was roughly determined by isodose curves taken photographically by putting a large film in a phantom and sending the x-rays into the phantom in the plane of the film. We did this experiment at the suggestion of Dr. H. Quastler, of the Carle Hospital Clinic in Urbana. Measurements with the densitometer on the photographic film indicated that the intensity of ionization diminishes to 50 per cent about 5 cm. from the beam axis. This gives a width of the beam at half maximum of about 10 cm. The surface of the phantom was placed 70 cm. from the target, and no cone was used in front of the betatron. It is a natural tendency of high-energy x-rays to proceed in the direction which the electrons producing them had when they struck the target.

Factors Concerned in the Abnormal Distribution of Barium in the Small Bowel[1]

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THE ROENTGEN appearance of the small bowel in neoplastic disease and in certain types of inflammation ordinarily can be correlated adequately with the gross pathological appearance of the involved segments. The factors concerned in the production of certain abnormalities, however, which have been grouped together under the term "deficiency pattern" have been the subject of considerable speculation and investigation. In the present study the clinical data in a group of cases which revealed this pattern were reviewed and certain limited experiments were carried out. The group consisted chiefly of 6 cases of the acute phase of granulomatous jejuno-ileitis, 24 of sprue, 13 of celiac disease, and 9 of definite avitaminosis.

The roentgen changes under discussion are: (1) variations in motility and tone, (2) dilatation of loops, (3) abnormal segmentation, (4) coarsening or obliteration of the mucosal folds, and (5) flocculation of the barium. The pattern is found in a variety of circumstances. It can be shown regularly in primary deficiency states and is seen occasionally in secondary deficiency complicating an existing gastro-intestinal lesion. It occurs in conditions such as pancreatic insufficiency and icterus, in which there may be interference with fat absorption, and in single cases of hyperthyroidism, hyperparathyroidism, and regional enteritis in which there is no known deficiency except such as might be attributed to diarrhea. The occurrence of the pattern in certain emotional and allergic states indicates that it can occur in the absence of known deficiency. The term "deficiency pattern," therefore, is a misnomer and might better be replaced by a detailed description of the findings in the individual case.

It is evident from our cases that an acute inflammatory process can produce a pattern which is indistinguishable from the so-called "deficiency pattern." Its occurrence in acute granulomatous jejuno-ileitis (Case 1), in the absence of clinical and laboratory evidence of nutritional deficiency, indicates that the pattern can be produced by a process consisting of inflammation, edema, and thickening of the submucosa with acute ulcerations in the mucosa (14). Thickening of the mesentery may or may not be of importance in the production of the pattern. There is a large number of cases in which the differentiation of atypical but primary sprue from nutritional deficiency secondary to chronic inflammation is difficult (Case 2). Because the disease of the small bowel is extensive and acute surgical episodes do not occur, exploration is not indicated, and pathological study is not available. The clinical similarity to the chronic phase of granulomatous jejuno-ileitis is sufficiently close, however, to suggest strongly that, even if primary nutritional deficiency is present, a chronic low-grade inflammatory process also will be found. It is likely that in these cases the local infiltration accounts for the small bowel pattern.

In sprue, on the other hand, although low-grade inflammatory changes usually are found, and occasionally a marked mucosal atrophy, the changes are mild. They consist of edema, congestion, round-cell infiltration, and fibrosis in the submucosa, atrophy of the mucosa, and degenerative changes in muscle and ganglion cells. There is neither rigidity nor stenosis. However, though the precise mechanism is unknown, considerable evidence can be elicited that these changes individually are capable of

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producing the abnormal roentgen findings. For example, edema alone can produce segmentation and unequally dilated loops, as is shown by the roentgen appearance of the small bowel in acute allergic enteritis in which there is an acute edema of the intestinal wall which returns to normal following the administration of adrenalin. Hypoproteinemia, as in nephrosis, is associated with edema of the submucosa, which probably accounts for the segmentation found in this disease. Segmentation, even in the absence of ascites, is seen also in cases of cirrhosis of the liver, a condition in which edema is present, and, in rare cases, phlegmonous inflammation. The investigations of Oettel and Thaddea (11) indicate that edema is an early finding in sprue. They showed that low values for plasma albumin with edema can exist for years before the appearance of gastro-intestinal symptoms.

Atrophy of the mucosa can account for the roentgen appearance of coarsening or obliteration of the mucosal folds. Kantor (6) was able to correlate closely mucosal atrophy and the roentgen appearance of "ironing-out" of the corresponding jejunal segment in a single postmortem case of sprue. That a pathological process limited to the mucous membrane can produce segmentation, dilatation and an "ironed-out" mucosal pattern is illustrated by one of our cases, in which the infiltration was due to amyloid. Accentuation of the jejunal mucosal pattern is not so easily explained, but may depend on the fact that the mucous membrane is the origin of many reflexes, disturbances in which modify muscle contraction.

The role of muscle damage itself, perhaps on a metabolic basis, has not been emphasized sufficiently. Fischer (2), for example, found hemofuscin in the muscularis propria in sprue. Klemperer (7) also noted this pigment in two cases with a sprue syndrome in which a "deficiency pattern" had been demonstrated previously. One was a typical case of nontropical sprue. The other was a case of lymphosarcoma of the small bowel which, clinically, presented a sprue syndrome. In the absence of sprue, hemofuscin has been found in the smooth intestinal muscle in only two other cases in this hospital. In one, there was an acute and chronic ileocolitis which was not striking and might have been secondary to diarrhea. This patient, however, had a hemorrhagic diathesis suggesting a deficiency of at least vitamin K. The other was a case of cholangitic cirrhosis with severe icterus. The only common denominator which suggests itself in these four cases is a disturbance in fat metabolism or absorption.

The response of the pattern in sprue to "specific" therapy is important. In our cases, a marked improvement was observed in 50 per cent of the cases following the administration of liver. There was some question whether the pattern ever returned completely to normal. Despite careful analysis of the clinical data, no correlation between response to therapy and the severity and duration of disease could be made out. Case 3 illustrates a satisfactory small bowel response. Certainly, the persistence of abnormalities despite profound clinical improvement is consistent with residual inflammatory disease, just as it is in granulomatous jejunoileitis. Our Case 4 also illustrates this point. In this case, there was no response to liver therapy. There was improvement in the pattern when the patient was given a celiac diet, but distinct abnormalities remained. Frequently steatorrhea disappears but the deficiency pattern does not change. This suggests local disease of the small bowel wall. If Hurst (5) is correct in assuming that paralysis of the muscularis mucosa is responsible for steatorrhea, disappearance of the latter should be associated with improvement, or at least change, in the appearance of the small bowel. The disappearance of steatorrhea did not change the pattern. Hence it is unlikely that the excess split fat is responsible for the abnormalities. The possibility that bowel content does influence the pattern to some degree is conceivable, nevertheless, since non-absorbable hydrocarbons, such

as mineral oil, result in a segmental distribution of the barium. Furthermore, excess fat in the form of cream added to the barium meal regularly produces a peculiar mottling similar to that seen occasionally in sprue (13).

The neurogenic theory has been ably set forth by Golden (3), who suggests that as a result of interference with or damage to the plexuses there is (*a*) a defective response of the circular and longitudinal muscles to the normal stimulus of intestinal content which produces changes in motility and tone as well as segmentation and (*b*) a defect in the function of the muscularis mucosa resulting in changes in the mucosal folds. Hurst (5) elaborated a similar thesis as regards sprue and celiac disease, suggesting that the paralysis of the muscularis mucosa results in a loss of the pumping action of the villi by means of which fat is conveyed in the larger lacteals. He suggests that there is a loss in the normal stimulation of Meissner's plexus. In this way, the entire mechanism of the small bowel pattern in deficiency states is related to the alteration in the nerve plexuses. This hypothesis is based upon the following evidence:

1. Histological evidence of damage to intramural nerve cells in experimental and clinical advanced deficiency states.
2. The importance of vitamin B in intracellular oxidation processes, and therefore presumably in normal nerve function.
3. The small bowel pattern in infants, which resembles closely the "deficiency pattern," and is thought to be due to incomplete development of the nervous system.
4. The possibility that motor disturbances in the intestine may result from nerve impulses arising outside the intestinal wall. The effect of emotional disturbance on the small bowel pattern is cited.
5. The pathologic changes in the intestinal wall occurring as the result of long continued nutritional deficiency seem to vary widely in different individuals but damage to the intramural nervous system is thought to be common to all.

In an investigation of some of the implications of this hypothesis in our group of cases the following results have been obtained:

1. The histology of the small bowel was reviewed. It became apparent that ganglion cell vacuolization must be interpreted with considerable caution. Vacuolization of the ganglion cells in Auerbach's plexus was observed commonly in cases in which there was no known deficiency (7). These changes were noted recently, for example, in an appendix which was removed routinely in the course of a hysterectomy. Furthermore, degeneration often could be accounted for by interference with circulation resulting from edema and infiltration, as Golden pointed out.

2. The importance of various components of the vitamin B complex in cellular metabolism is not questioned. It is very likely that normal nerve function is not maintained in an advanced deficiency. Furthermore, in deficiency of certain components, such as thiamine, there is a predilection for the production of nerve damage. There is also considerable evidence, however, that the metabolism of other tissues is seriously disturbed, which might be just as potent in producing derangement of the small bowel. It seems significant that in the clinical cases of vitamin B deficiency in which peripheral neuritis is a feature, and in which, therefore, degeneration of the visceral nerve plexuses might also be expected, small bowel abnormalities are not frequent. Either, therefore, a coincidental visceral neuropathy is absent or it is not sufficient to produce changes in the small bowel pattern. Pernicious anemia is another condition in which peripheral neuritis is frequent but a "deficiency pattern" has not been found. On the other hand, if the pattern in sprue is due to a visceral neuropathy, the infrequency of peripheral neuritis in this condition is noteworthy. Woltman and Heck (16) reported clinical signs in 11 out of 29 cases, which, however, is a higher incidence than

we have encountered. Certainly lack of vitamin B is not essential to the production of the "deficiency pattern," since typical changes have been observed in cases of pancreatic insufficiency (12) in which there is no known deficiency of this vitamin.

3. We have attempted, by the administration of drugs, to investigate, in a limited way, the importance of the autonomic nervous system in the formation of the small bowel pattern in sprue. If there is degeneration of some of the parasympathetic plexuses in the small bowel wall, it would be anticipated that interference with vagus action would produce a somewhat similar response in the normal small bowel. It has been previously noted, however, that atropine to tolerance does not change the pattern (13). Furthermore, we have had the opportunity to observe the small bowel in one case following bilateral vagotomy and in another in which the vagi were sectioned above the diaphragm. While these operations did not remove all of the vagus action, there must have been serious impairment. In each instance a slight delay in transit time of the barium was noted. Where the vagus was sectioned above the diaphragm, a slight tendency to segmentation appeared; in the other instance no abnormality was seen. In neither case was there a change in the mucosal pattern.

Interference with the vagus activity in cases showing a deficiency pattern also yielded interesting results. When hyperactivity of the parasympathetic action is present, it can be blocked by atropine, a drug which acts at the end organ. In one case, for example, infestation with Strongyloides and Schistosoma resulted in a nonspecific irritation of the small bowel, the roentgen appearance of which was much like the usual deficiency pattern. This effect was counteracted completely by the administration of atropine. It is reasonable to suggest that in sprue, if segmentation is to be accounted for by degeneration of some of the ganglion cells, disturbed activity of the parasympathetics should be present, at least in those instances in which the degeneration is proceeding actively. Hence atropine should modify the small bowel pattern in these cases. In 6 patients with sprue who received atropine to tolerance, there was no effect on the sprue pattern. In 4 of these patients the pattern returned to normal following liver therapy, indicating that the factors producing the deficiency pattern had not induced permanent changes. In only one case (Case 5) there was reduced irritability following administration of atropine, but no change in segmentation and flattening of the mucosa was observed, the implication being that hyperirritability of the parasympathetics, when present, is an added phenomenon and can be blocked by atropine.

These patients were also given benzedrine in doses which in normal subjects produce no change in the pattern but do delay transit time (13). There was no effect whatsoever on the "sprue" pattern. This drug ordinarily has a sympathomimetic action, in addition to an atropine-like action, and might be expected further to modify reflexes if they were already disturbed.

4. The small bowel pattern in infants which resembles a deficiency pattern has been explained by "incomplete development of the nervous system," implying that the autonomic system also is not fully developed. Mackie (9), for example, cites as evidence the presence of a positive Babinski reflex in infants. This indication of incomplete myelinization of the pyramidal tracts, however, probably has no relation to the vegetative nervous system, which is phylogenetically the older system and whose postganglionic fibers never become myelinated. The observations of Zwerling and Nelson (17), who found a deficiency pattern in 38 out of 77 normal children between the ages of three months and eleven years, are of great interest. In only 5 cases was a completely normal adult pattern found, the earliest being in an infant of eleven months. If the infantile pattern is due to incomplete development of the autonomic system, we must assume that development is not completed in many cases until well along in childhood,

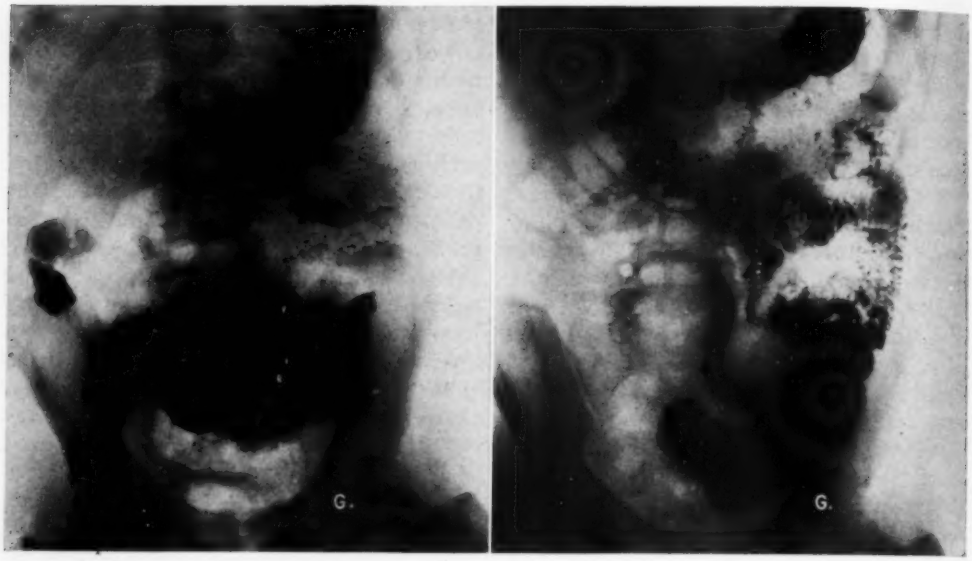

Fig. 1. Case 1: Granulomatous jejuno-ileitis. Appearance of stenosis and rigidity in two years. Original pattern could not be differentiated from "deficiency pattern."

which certainly is not substantiated when comparison is made with other autonomic functions.

5. The possibility that the infantile pattern is due to a modified muscle action as the result of a heightened adrenalin sensitivity of the end organ in young children, as in young animals, should be seriously considered. Although Zwerling and Nelson noted no change when their examination was repeated in 5 cases and when the children were less emotionally upset, a hormonal mechanism is likely to be important in the formation of the childhood pattern. For example, we have been able to produce an abnormal pattern in a sensitive adult by the use of adrenalin.

CONCLUSIONS

1. The term "deficiency pattern" has been used loosely to designate the roentgen appearance of the small bowel when there is segmentation with changes in motility, tone, and mucosal pattern. There is no definite reason, at the present time, to assume that these findings are necessarily variations of a single pattern with a common pathogenesis.

2. Edema and infiltration of the submucosa, atrophy of the mucosa, muscle damage, and nerve degeneration, modified at times by abnormal bowel content and by unusual hormonal or nervous stimuli, individually are sufficient to produce the "deficiency pattern." In some diseases, such as granulomatous jejuno-ileitis and allergic enteritis, there is no reason to suspect that any other factors are operating.

3. In nutritional deficiency, although the local inflammatory changes are sufficient to produce the abnormal small bowel pattern, a primary tissue disturbance may be produced by the deficiency and, as a result, interference with the normal intestinal reflexes. However, the pathway or tissue through which these deficiencies may operate to produce the small bowel abnormalities remains undetermined.

4. There is experimental evidence (4) which suggests that the pattern can be produced by deficiency in certain vitamin B components. There is no established proof concerning which components are lacking either in experimental or human disease.

CASE REPORTS

CASE 1 (No. 481165, service of Dr. G. Baehr): R. C., a 19-year-old male, was admitted in 1938 complaining of diarrhea with 10 to 12 bowel movements daily, which were occasionally bloody. Abdominal pain was present, with loss of 15 lb. in weight. The patient was acutely ill, his temperature being septic in type. A mild secondary anemia and moderate leukocytosis were present. Stools were positive to guaiac test. On one occasion, a Flexner dysentery bacillus was cultured from the stool and a positive blood agglutination for the same organism was obtained.

Barium enema examination showed slight irritability and loss of haustration of the descending colon. A barium meal study revealed a coarsening of the jejunal pattern with ironing out in some areas, segmentation with dilatation throughout the small bowel, with flocculation of the barium. The terminal ileum appeared involved. During the next two years there were several mild recurrences. The small bowel disease progressed to rigidity and stenosis of several loops, indicating chronic granulomatous jejuno-ileitis. (Fig. 1.)

CASE 2 (No. 429286, service of Dr. G. Baehr): B. W., a female, aged 31 years, was admitted in September 1938 with a history of diarrhea for two years. Bowel movements occurred 12 to 14 times daily and recently had been bloody. Physical examination revealed early clubbing and ankle edema. There were physical signs of mitral stenosis and insufficiency. During the hospital stay, aphthous ulcers were seen in the mouth occasionally. A cryptitis with an anal fissure and hemorrhoids were noted. The patient had received x-ray treatment to the neck for hyperthyroidism eleven years previously.

Blood studies showed a mild secondary microcytic hypochromic anemia; blood platelets 240,000; reticulocytes less than 0.5 per cent; total blood protein 5 gm. per cent; serum calcium 8.4 mg. per cent. An oral glucose tolerance test revealed an almost flat curve. The intravenous test was normal. The gastric content showed no abnormality. Fat in the stool varied between 25 and 39 per cent of the total dried content. Stool cultures were negative.

Barium enema examination showed no definite abnormalities. Barium meal studies revealed segmentation with dilatation of the small bowel loops, particularly the ileum. There was a moderate clinical improvement on a high-protein, low-fat diet, with vitamin B complex and parenteral administration of liver. There was no change in the appearance of the small bowel pattern. The classification of this patient's condition appears to be impossible at this time. The available evidence can be considered as pointing to inflammatory or deficiency disease. (Fig. 2.)

CASE 3 (No. 451604, service of Dr. B. S. Oppenheimer): R. F., male, aged 54 years, was admitted Jan. 24, 1940. He was a Porto Rican laborer who had lived in the United States for twelve years. He had yellow fever at twenty and an operation on inguinal buboes twenty-eight years prior to admission. Six months before admission he began to suffer from weakness, anorexia, and diarrhea, with frequent watery stools and loss of 29 lb. in weight. Two months before admission, bloating, borborygmi, and diarrhea became severe.

Fig. 2. Case 2: Deficiency pattern presumably due to local inflammatory disease Clinically the case is indistinguishable from non-tropical sprue.

The tongue was beefy red. There was no definite atrophy or glossitis. The pharynx was pale, the chest clear. There was a slight clubbing of fingers and toes.

Blood studies showed: hemoglobin 63 per cent; color index 1.2; white cells 5,900; platelets 140,000; hematocrit reading 21 per cent. Reticulocytes were less than 0.5 per cent, total blood protein 6.2 gm.; albumin 4.5 gm.; phosphorus 3 mg. per cent. The Janney test revealed a flat curve. Gastric content showed free hydrochloric acid 10, total 30. The stools were yellowish and frothy but no blood or mucus was present.

A gastro-intestinal roentgen series revealed segmental dilatation with coarsening, decrease to absence of mucosal pattern, flocculation, and hypomotility. The changes were severe. The colon showed irregular mottling, presumably due to abnormal content.

The patient received liver intramuscularly twice weekly and a high-protein, low-fat diet was recommended. There was marked clinical improvement with disappearance of steatorrhea. The patient has

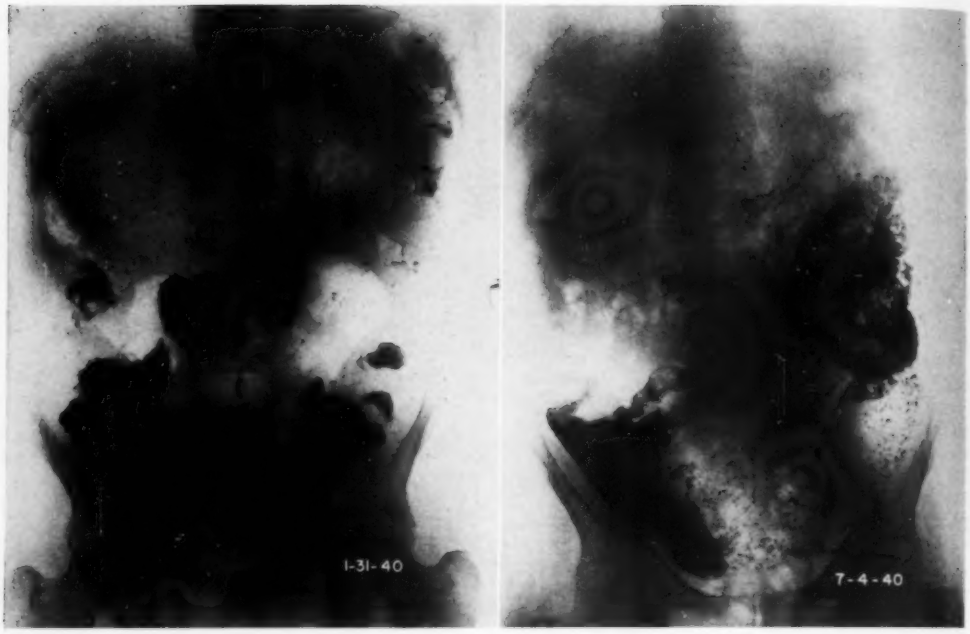

Fig. 3. Case 3: Non-tropical sprue showing marked improvement in the small bowel pattern following specific therapy.

Fig. 4. Case 4: Non-tropical sprue. No response to liver therapy. Marked improvement on a celiac diet. (Roentgenogram on the left was made in 1942.)

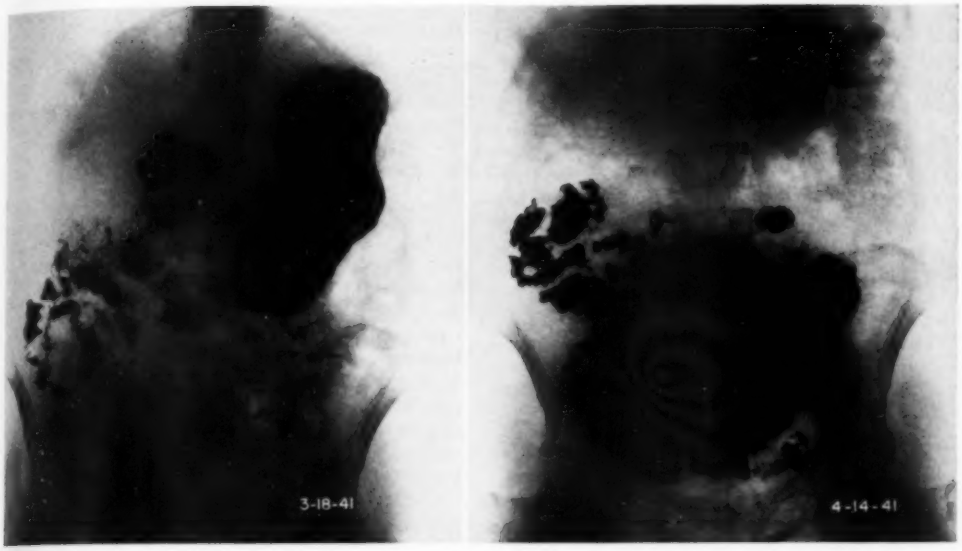

Fig. 5. Case 5: Non-tropical sprue. Reduction in irritability following atropinization. The basic "sprue pattern" was irreversible.

remained asymptomatic for two years. His tongue is no longer beefy but there are some signs of atrophy. The small bowel pattern has become almost normal. (Fig. 3)

CASE 4 (No. 468415, service of Dr. G. Baehr): E. C., an American woman aged 45 years, entered the hospital with a story of intermittent diarrhea for twenty years. The past history revealed a visit to the tropics at the age of twelve and an episode of diarrhea in Italy at the age of twenty-six. An appendectomy and cholecystectomy had been performed previously. The diarrhea was associated with yellowish-white foamy stools. In addition there was a generalized papular erythematous eruption. The patient had been on an "anticolitis" diet which was notably deficient in fresh fruit and vegetables.

Blood studies showed hemoglobin 90 per cent, red cells 4,400,000, with definite macrocytosis; total protein 5.5 gm. per cent; calcium 8.7 mg. per cent; phosphorus 3.1 mg. per cent. The stools were negative to the guaiac test; fat accounted for 57 per cent of the total dried content. An oral fat tolerance test showed practically no absorption. An oral Janney test yielded a flat response.

Roentgen study showed hypomotility of the small bowel, pronounced segmentation with dilatation of the small bowel loops, flocculation of barium, coarsening of the mid-jejunal pattern, and intestinal fluid level. Benzedrine had no effect upon this pattern except for a slight increase in motility.

The patient was given a celiac diet with marked improvement in the clinical symptoms. The stool fat dropped to 25 per cent of the total dried content. The oral glucose tolerance curve showed improved absorption. After a reasonable interval, the patient was placed on a regular diet, with liver given intramuscularly. There were definite exacerbation of the symptoms and recurrence of steatorrhea. Return to a celiac diet without any other therapy has maintained the improvement in the patient's condition. Re-examination of the small bowel fourteen months later showed great improvement. Only slight abnormalities could be noted in the pattern.

In this case response, clinically and roentgenologically, to a celiac diet was evident, but there was no response to liver alone. The case demonstrates a reversible deficiency pattern which was not changed by the administration of benzedrine, a drug with a sympathomimetic and, in addition, an atropine-like action. (Fig. 4.)

CASE 5 (No. 470112, service of Dr. G. Baehr): M. R., Porto Rican woman, aged 68, complained for three years of esophageal and epigastric burning, weakness, anorexia, and loss of weight. During this time, despite intensive liver and iron therapy, deterioration continued. Diarrhea occurred once only but the stools were described as occasionally foamy. Physical examination revealed a mild glossitis.

A hyperchromic macrocytic anemia was present with a hemoglobin of 38 per cent and a red cell count of 1,200,000. The bone marrow was described as hyperplastic and predominantly erythroid, a type which often responds poorly to liver therapy. The stool was negative to the guaiac

test. Fat constituted 46 per cent of the total dried stool content. The oral Janney test gave a flat response. Intravenous Janney test showed a normal response. Examination of the gastric contents showed free hydrochloric acid 10; total 30. The total blood protein was 6.3 gm. per cent, albumin 4.5 gm. per cent, globulin 1.8 gm. per cent, calcium 8.3 mg. per cent.

Small bowel study showed hypomotility, coarsening, slight dilatation of ileal loops, a tendency to segmentation and flocculation. Fluoroscopy revealed areas of hyperirritability. Atropinization as well as administration of benzedrine reduced this irritability but did not change the basic pattern.

Therapy with parenteral liver administration and iron produced slight improvement, which, however, was greater when the patient received a celiac diet. (Fig. 5.)

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DISCUSSION[1]

Ross Golden, M.D. (New York): Doctor Sussman has presented certain ideas on the disturbances in the motor function of the small intestine which are not in accord with certain ideas I have acquired as a result of observations on patients and from the literature. Therefore, his paper has been more than usually stimulating. Inasmuch as I did not have the opportunity to discuss his paper at the time of its presentation, I would like to take this means of commenting on a few of several points which are worthy of attention.

Doctor Sussman does not like the term "deficiency pattern," and I don't blame him. This expression grew up in our Department; I don't quite know how. It was originally used because the early cases were actually deficiency states. We recognized long ago the non-specific nature of these intestinal disturbances and that, from the appearance, the cause cannot be determined. However, as the term expresses an idea in two words, it continues to be used. We would be delighted to have Doctor Sussman give us a better one. The term "irritation pattern" was used many years ago, I believe by Mills, and perhaps would be better.

Doctor Sussman believes that, because the phenomena are produced by a number of different causes, it is inadvisable to assume a common mechanism, and that there are undoubtedly a number of mechanisms involved. I don't know in exactly what sense he used the term "mechanism" but am convinced, for this particular reason, *i.e.*, because these physiologic disturbances can originate in so many different ways, that there must be somewhere a common denominator, a point—so to speak—through which these different forces must act to produce similar disturbances in intestinal physiology. After reviewing the available evidence (see Abnormalities of the Small Intestine in Nutritional Disturbances: Some Observations on their Physiologic Basis," Carman Lecture. Radiology, **36:** 262–286, March 1941), it seemed to me that "a possible, if not the most probable" common denominator is the intramural nervous system. This suggestion was presented as a working hypothesis, not as a proved fact. Doctor Sussman feels that the evidence is decidedly against that possibility and suggests other possibilities, the most important being the muscle itself. At this point, it seems desirable to review briefly two or three fundamental facts in intestinal physiology.

[1] Prepared for but not presented at the meeting.

In 1899 Bayliss and Starling showed, after paralyzing the intramural nervous system in the dog's intestine with cocaine, that the rhythmic pendulum movements were unchanged, but that the peristaltic movements by which a bolus was passed along were completely disorganized. They concluded that the pendulum movements are myogenic in origin and that the peristaltic movements are co-ordinated reflexes depending upon the intramural nervous system. This view of the relation of the intramural nervous system to the muscular activity of the intestine is accepted today. By repeatedly passing a bolus through a loop of dog's intestine they produced fatigue effects, and the earliest evidence of fatigue was failure of relaxation of the wall below the bolus. Alvarez (An Introduction to Gastroenterology, p. 196) states: "An important function of the ganglion cells in the plexuses is apparently to keep the muscle from contracting into a hard knot." The ability of the wall to relax is just as important in its normal function as the ability to contract and apparently depends upon the intramural nervous system. It is the failure of segments to relax normally which produces the abnormal segmentation which is the most constant phenomenon in the disordered intestinal physiology under discussion.

Doctor Sussman introduces the effect of adrenalin on the intestine as evidence against the hypothesis that the intramural nerves are the common denominator because this drug acts directly on the muscle, not through the nerves, and yet produces a deficiency pattern. It is now generally accepted that the sympathetic nerves affect the muscle by producing, at the nerve endings, a chemical which Cannon calls "sympathin" and which, according to Sollman, is indistinguishable from adrenalin. So, although adrenalin does not work through the nerves, the nerves work through adrenalin, which seems to make reappraisal of this evidence desirable.

The demonstration of hemofuscin in the intestinal muscle cells in sprue by Doctor Klemperer is very interesting. I hope more information along this line will be forthcoming. But the fact of muscle damage does not eliminate the possibility that the common denominator is the intramural nervous system. In one of our cases of non-tropical sprue, degenerated muscle cells were demonstrated along with degenerated nerve cells.

Doctor Sussman reviews other pathologic changes as possible mechanisms for producing the deficiency pattern. The most important is submucosal edema, because that is present in hypoproteinemia, and we found it in a case of subacute yellow atrophy of the liver. But the question must be asked: "How does the submucosal edema affect the physiology of the intestinal musculature?" Is it entirely mechanical? It seems unlikely, because of the evidence of incoordination of movements. Doctor Sussman mentions excessive fat within the lumen as a possible source of the disturbance—but how is the effect accomplished? The same question must be asked about all the pathologic changes mentioned. There must be a mechanism through which the effect is produced.

The intestine of the normal newborn infant is unable to handle its contents as does the normal adult intestine; it shows no or very few and low mucosal folds in the jejunum and in a few minutes after the entrance of barium extensive segmentation appears, indicating incoordination of the reflex mechanism. Doctor Sussman feels that the evidence that the intramural nervous system is concerned in these phenomena is inconclusive. Inasmuch as it is generally agreed that the nerves in the wall are the medium through which the propulsive movements are coordinated and which are responsible for the ability of the wall to relax, it seems to be at least a logical hypothesis.

It must be borne in mind that all nutritional disturbances are complicated and are relatively little understood as yet. Why is beriberi "wet" in one case and "dry" in another? And yet both are beriberi. Why does one patient with sprue have hypoproteinemia, another hypocalcemia, another both, and another neither, and yet all are sprue? We must not be surprised to find vagaries in the conduct of the intestine in these conditions. The intestine, important as it is, undoubtedly does not tell the whole story in nutritional disturbances. But we must recognize the intestinal disorders by proper roentgen methods and accept them as nonspecific indications of certain possibilities. It seems to me that our thinking about the complicated problems of disordered intestinal physiology will be less confused if we postulate a common denominator through which the effects are produced. Whether it be in the muscle or in the intramural nerves, or possibly in both, the most important thing is that it seems to lie within the intestinal wall.

A great deal remains to be learned about the small intestine and I hope Doctor Sussman will continue his experiments on patients with disordered intestinal physiology and will tell us more about them in the future.

Marcy L. Sussman, M.D.: Ordinarily the roentgen findings in the presence of diseased abdominal viscera can be correlated directly with the gross pathological appearance. Disturbances in peristalsis and interference with the propagation of the contraction wave can be explained adequately by the local disease. For example, in granulomatous jejuno-ileitis, the infiltration of the wall interferes with normal contraction and relaxation and results in rigidity. In cases of nutritional deficiency, however, the gross changes in the small bowel wall often are not sufficient to account for the roentgen appearance. Under these conditions Doctor Golden suggests that the segments fail to relax normally because of degeneration of the intramural nerve plexuses. There is no doubt that the nerve plexuses

are a very important factor in the control of intestinal movements but I think Doctor Golden will agree that the plexuses are only one part of the reflex arc and that the same end-result may come from a disturbance in any part of the arc. In other words, if edema of the walls and atrophy of the mucosa inhibit the origin or pathway of reflex impulses, the effect would be the same as blocking the impulses at the nerve plexuses. Muscle degeneration also would interfere with the reflex arc as well as disturb those movements of myogenic origin. In considering whether degeneration of the nerve plexuses is the primary factor, we must decide first whether it is a reasonably constant finding in the cases of nutritional deficiency which are associated with an abnormal small bowel pattern and, second, whether or not a "deficiency pattern" occurs ordinarily when degeneration of the nerve plexuses is present. I have demonstrated that the presence of nerve cell vacuolization is not necessarily associated with an abnormal small bowel pattern. Furthermore, in beriberi, in which Vedder reported extensive degeneration of the sympathetic system in addition to central and peripheral neuropathy, there has been no report to my knowledge that abnormal small bowel changes are common.

Physiological investigation of the problem is confusing because the precise nature of the deficiency remains obscure. Doctor Golden and Doctor Lepore have shown that deficiency of the entire vitamin B complex is associated in man with an abnormal small bowel pattern. May, McCreary, and Blackfan have reported improvement in the small bowel pattern in celiac disease following the administration of crude liver extract and vitamin B complex. I have illustrated the marked improvement which may occur in sprue following liver therapy. There has been no report, however, that a "deficiency pattern" occurs in man as the result of the deficiency of any of the known isolated components. Even in the more complicated deficiencies, in which there may be a predominant deficiency of one factor—clinical pellagra perhaps fits into this classification—a "deficiency pattern" apparently has not occurred with sufficient regularity to have been commented upon in the literature except possibly for disturbances in gastric and small bowel emptying. The fact that several vitamin B components have been shown to be involved in cellular oxidative processes, and therefore in nerve cell physiology, cannot be taken as proof that when the component associated with the production of a "deficiency pattern" is identified, its lack will be found to act through the nerve plexuses. Certainly when parasympathetic activity is blocked with atropine, there is no change in the pattern in sprue. On the other hand, May, McCreary, and Blackfan reported that mecholyl, a vagal stimulator, given in cases of celiac disease, resulted in the disappearance of the clumping in the small bowel. We are now investigating the effect of this drug in sprue.

Doctor Golden's suggestion that the small bowel pattern in infants is due to incomplete development of the intramural nervous system is difficult to confirm or deny. I think it may be assumed that the autonomic nervous system is complete anatomically at birth. Dr. Albert Kuntz answered my query on this subject as follows: "The plexuses in the wall of the alimentary canal undoubtedly represent one of the most primitive parts of the nervous system. While we have no specific data regarding the time at which they become functional, I think it may be assumed that they are functional a good while before birth." A variation in any part of the reflex arc in the infant as compared with the adult will produce the same effect as a change in the plexuses. I know no convincing reason for choosing the intramural plexuses.

Doctor Golden's statement regarding the wide variation in the symptomatology of sprue is answered, at least in part, by the fact that many of the cases so classified are not sprue. Reduced glucose and fat tolerance, macrocytic anemia, and glossitis are non-specific responses. Doctor Golden states that the small bowel pattern also is not specific. However, just as various types of glossitis are now being classified and related to individual deficiencies, so it may be that there are small but important differences in the roentgen appearance of the small bowel which have not yet been identified by our present rather crude analysis and which will permit a classification into specific patterns.

Because these important considerations remain unsolved, I have suggested that it is premature to regard primary nerve degeneration as the common denominator. There is no doubt whatever that the integrity of the autonomic system, including the entire reflex arc, is essential for normal functioning of the small bowel, and to this extent it is obvious that changes in the intramural nerve plexuses must be considered as one of the possible sites of primary disturbance.

X-Ray Therapy in Fluoroscopy[1]

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PRIOR TO THE discovery by H. J. Muller in 1927 of the high potency of the roentgen ray in the production of hereditary changes, radiologists in general measured the harmful effects of this radiation in terms of gross skin and tissue damage and its effects on fertility and on the hematopoietic system and certain of the endocrine glands. These effects were frequently observed during the lifetime of persons who were exposed to sufficient x-radiation and were thought to be the only ones occasioned by such exposure. Muller's original work was done with *Drosophila melanogaster* (fruit fly) and revealed that even very small doses of x-ray (10–15 r) produced changes in the germ cells of these insects which not only caused first and second generation mutations, but transmitted these effects to succeeding generations. The changes produced were many, varying from slight anomalies to gross deformities incompatible with life. In subsequent generations the mutations occurred most frequently where the ancestors of both male and female had been irradiated, but many instances were observed where the ancestors of only one parent had been irradiated, and where the parents themselves were entirely normal appearing individuals. While 10–15 r produced the above changes, 30–40 r were necessary in order regularly to double the number of mutations over those observed in control groups.

Following Muller's report, numerous investigators obtained similar results, using a variety of plants and animals. The problem assumed a more serious aspect when it was found that radiation necessary to produce these mutations was cumulative, and the 10–15 r necessary to produce changes in the hereditary factors could be administered in small fractional doses over the period of reproductive activity of the individual's life. Furthermore, since these hereditary factors are naturally transmitted from parent to progeny, the effect of the radiation could be cumulative not only throughout the reproductive life of one individual but through successive generations.

To make the statement that such changes occur from the clinical use of x-ray would not be entirely true. Even if the amount of radiation thus used were sufficient to produce alterations in the chromosomes, in most instances it would not be applied to the whole organism or to the gonads, where the cells containing the hereditary factors are located. There can be no question, however, that possibilities of serious change do exist from the clinical use of x-radiation, provided sufficiently large amounts of radiation reach the gonads of the patient or operator. Because of this, it is important that a knowledge of the amount of radiation incidentally given to patients undergoing x-ray examinations should be known as accurately as possible, so that adequate steps can be taken to prevent such radiation reaching the gonads, or to limit it to the lowest possible amount.

In recent years there has been a rapid increase in the number of fluoroscopes used by practitioners as a whole. Prior to the development of the Coolidge tube, fluoroscopes were exceedingly difficult to operate under constant conditions, and the output of radiation from the old machines varied over a considerable range. The advent of this new tube made possible the construction of equipment which could produce a given x-ray intensity with fair constancy and could be easily managed by physicians without special training. Still further refinement of design and construction has recently resulted in the mass production of

[1] Read before the Radiological Society of North America, at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec. 1–5, 1941.

fluoroscopes, the reduced cost of which has made them easily available to all. Naturally many gastro-enterologists, cardiologists, internists, and general practitioners have acquired these useful and intriguing instruments. The number of physicians who have so equipped their offices may be judged by the fact that there are approximately 1,200 fluoroscopes in use in one large eastern city where there are approximately 4,700 registered physicians. In that locality there is approximately one fluoroscope to every four practising physicians.

Conversations with men who have these units indicate that much use is made of them, and that in many instances fluoroscopic observation is a part of the examination of almost every patient. When these examinations have been completed the examiner, who in most instances has no knowledge of the output of x-radiation or the biological effects therefrom, has no definite idea as to the total time of exposure. In an attempt to limit the time of operation some manufacturers have equipped their fluoroscopes with timers which limit the total exposure to a predetermined number of minutes. Where this is done, the manufacturer or engineer installing the apparatus estimates grossly the safe operating limits of the machine, usually in terms of skin or erythema units. The timer is then set so that, as far as skin damage is concerned, a relatively safe exposure results. We are informed that most of these timers are set to deliver a total dose of 150 r to the panel or skin, where the skin is in contact with the panel. Such timers, if properly used, reduce the dangers incident to fluoroscopic examination. In many instances, however, the timers are reset when the examiner wishes to observe the patient for a longer period. Furthermore, the full time of exposure (150 r) may be directed over the female pelvis, delivering a very large dose to the ovaries, or the exposure may be entirely limited to the thorax with no resulting gonadal irradiation.

Many roentgenologists have made measurements of their fluoroscopes and have determined the number of roentgens which reach the patient under certain conditions, *i.e.*, the conditions prevailing at the time of the measurements. These conditions, however, are not exactly met in routine work, and in some instances are not even approximated.

In order to determine accurately the amount of radiation to which persons undergoing routine examinations were actually exposed, one of the fluoroscopes at the Long Island College Hospital was equipped with an ionization chamber connected to a Braestrup irradiometer. An interval timer was then connected in the foot-switch circuit, which measured, accurately and cumulatively, the total fluoroscopic exposure.

The fluoroscope on which these instruments were mounted was approximately twelve years old. A 30-milliampere radiator tube and fluoroscopic screen of the ordinary type were used. With the routinely used factors of 88 kv.p., 3 ma., and a target-panel distance of 25 cm., the radiation output of the x-ray tube as measured in air and calculated at the skin level was found to be 30 r per minute. The use of 4 ma., with an output of 40 r per minute, was formerly used but discarded in favor of the lower value when it was found that satisfactory screen illumination could thus be obtained.

A number of variable factors were found that required correction in order to insure a constant output. When the machine was set as accurately as possible for 3 ma. and the prereading voltmeter adjusted to give a secondary voltage of 88 kv.p., the output was found to vary from 25 to 40 r per minute. These variations were occasioned by inaccuracies in the instruments furnished on the usual fluoroscopic equipment and variations in line voltage and line conditions producing fluctuations in radiation output. Where milliamperage was not carefully adjusted prior to each fluoroscopic examination, the radiation output varied as much as 100 per cent; even with careful setting, variations as high as 30

TABLE I: ACTUAL (r/min.) AND PERCENTAGE DOSES AS MEASURED WITH ORIGINAL EQUIPMENT

	Small Field (75 sq. cm. at the skin)		Large Field (208 sq. cm. at the skin)	
Skin dose (including back-scatter)	110%	33.0 r/min.	112%	33.6 r/min.
Dose at 5 cm. depth	26%	8.6 r/min.	30%	10.8 r/min.
Dose at 10 cm. depth	9%	2.95 r/min.	12%	3.95 r/min.

per cent were common. Close observation of the meters during fluoroscopy revealed the fact that the primary voltmeter in the filament circuit showed considerable variation, which produced changes in the milliamperage. Radiation output was also found to vary in different positions of the fluoroscope due to changed contact in the reels and connections. In order to reduce these variations, a heavy line was run to the fluoroscope, the reel contacts were kept cleaned and tight, and the output of the machine was frequently checked during the examinations. The difficulties encountered in maintaining a constant output of the fluoroscope even when special attention was given to the various possible sources of error indicated quite definitely that the average instrument in routine use cannot be relied upon to deliver accurately a predetermined dose, particularly when operated by one unfamiliar with the physical factors involved.

For three years many fluoroscopic examinations were observed with the apparatus described. Instead of being set at a certain milliamperage and voltage, the fluoroscope was adjusted for an average radiation output of 30 r per minute at a fixed voltage, prior to the examination. The time consumed for each examination was accurately recorded and the dosage was determined by multiplying the time in minutes by the number of r per minute administered.

At the end of the three-year period modern equipment was installed and one of the fluoroscopes was equipped with an irradiometer and timer. In the new apparatus the distance from the target of the x-ray tube to the panel was 38 cm. instead of 25 cm. as on the old machine, and the screen was a Patterson Type B, which was considerably more brilliant than that formerly used. The added brilliance of this screen and the increase in target-panel distance made it possible to achieve satisfactory illumination at a much lower radiation output. Varying the voltage according to the density of the patient, from 70 to 84 kv.p., and using 3 ma., produced an average output of 15 r per minute as measured at the panel.

The average exposure times for the various types of fluoroscopic examination were from one to four minutes for thoracic examinations; three to eight minutes for gastric and upper intestinal fluoroscopies; from one and one-half to four minutes for colon examinations. Because of the fact that colon examinations were made on practically all patients receiving gastric studies, the sum of the two fluoroscopic times should be considered as the total for complete gastro-intestinal examination. The dosage for the combined studies was administered over a period of four days, the upper tract fluoroscopy being done on the first day, the colon study on the fourth.

For purposes of measurement, two field sizes were used. The small one was 225 sq. cm. and was determined by measuring the averages of contracted fields of observation on the screen. The large field, 625 sq. cm., represented the average measurement of the screen area used during the initial survey. Computing the area at the level of the panel, it was found that 75 sq. cm. of skin was exposed when the small area was used, and 208 sq. cm. with the larger field. With the old equipment, the percentage dose and actual dose in r per minute delivered at the skin and depths of 5 and 10 cm. were measured. The results are shown in Table I.

The amount of radiation reaching any particular area of skin could not be ac-

curately determined because the exposure was not constantly directed at any one area.

Using the figures given in the table as a basis, the results of 1,454 fluoroscopic examinations were studied: 232 of these were made on the old equipment and 1,222 on the new. The doses delivered during the course of examination of the chest are presented in Table II.

TABLE II: DOSES IN ROENTGENS DELIVERED DURING FLUOROSCOPIC CHEST EXAMINATIONS

	Small Field (75 sq. cm. at the skin)	Large Field (208 sq. cm. at the skin)
Skin dose	33–132 r	33.6–134.4 r
Dose at 5 cm. depth	8.6–38 r	10.8–43 r
Dose at 10 cm. depth	3–12 r	3.95–15.8 r

In gastro-intestinal examinations, where exposures of from four and one-half to twelve minutes were employed, the doses shown in Table III were delivered.

TABLE III: DOSES IN ROENTGENS DELIVERED DURING FLUOROSCOPIC GASTRO-INTESTINAL EXAMINATIONS

	Small Field (75 sq. cm. at the skin)	Large Field (208 sq. cm. at the skin)
Skin dose	148–396 r	151–403 r
Dose at 5 cm. depth	38.5–102 r	49.0–130 r
Dose at 10 cm. depth	13.3–35.5 r	17.8–47.5 r

With the use of the new equipment, in which the target-panel distance was increased from 25 to 38 cm., the increased brilliance of the Patterson Type B screen permitted the use of 15 r in air or 16.5 r at the skin. The dosage both at the surface and in the deep tissues was, therefore, halved.

So far, only the radiation incident to the fluoroscopic portion of the examination has been considered. It must be remembered that radiation is also used in the making of films; particularly in gastro-intestinal examinations, where a great many pictures are taken. Most of these are, of course, of the upper abdominal structures, but in our routine gastro-intestinal studies, at least six exposures are made in which the whole abdomen and pelvis are included. According to Braestrup, the average dose in roentgens for each 100 ma.- second skin exposure at 80 kv.p., assuming 0.5 mm. aluminum added filtration and approximately 36 in. target-skin distance, is 4.3 r at the skin, 1.5 r at 5 cm. depth, and 0.54 r at 10 cm. depth. Assuming each individual exposure with the above settings to be a quarter of a second, the exposure of the whole abdomen, including pelvis, would equal 150 ma. seconds. This would result in a dose of 6.5 r to the skin, 2.25 r at 5 cm., and 0.82 r at 10 cm. While these doses are small, when they are added to those delivered by fluoroscopy, particularly as gastro-intestinal examinations are frequently repeated, the total amount of radiation delivered to the gonads may reach serious proportions. The fact that the hereditary influences of radiation have been shown to be cumulative throughout the fertile lifetime of the individual adds to the seriousness of the situation.

It can readily be seen, then, that even with our new equipment and markedly reduced dosage, radiation in excess of the 10 r which has been shown experimentally to produce hereditary changes in *Drosophila* eggs and small mammals, can readily be administered to the ovaries, and in the presence of unrecognized early pregnancy, the whole fetus together with gonadal tissue of both parent and offspring might easily be damaged. In the case of a colon examination, where a greater part of the radiation is delivered to the pelvis, this danger is increased.

Recently, Braestrup measured the output of a number of vertical, horizontal, and tilt fluoroscopes in various institutions and offices at the settings which their operators routinely employed. The voltages varied from 66 to 95 kv.p. and, of course, in some of the self-rectified units, was not definitely known; 5 ma. was constantly used in all measurements. Filtration varied from 0.5 to 1.0 mm. aluminum, and the target-panel distance from as little as 17.8 cm. to 43.8 cm. Measurements at

the panel showed considerable variations in the r output, from a low of 6.8 r per minute on a self-rectified unit of unknown voltage using 1 mm. aluminum filtration and a target-panel distance of 33 cm. to a high of 127.6 r per minute on a self-rectified unit using an unknown voltage, 0.5 mm. aluminum filtration, and a target-panel distance of 17.8 cm. The latter machine, when studied after increasing the target-panel distance from 17.8 to 30.5 cm. and the filtration from 0.5 to 1.0 mm. aluminum, showed a decrease in radiation output to 23 r per minute at the panel.

The fluoroscopic exposures reported in this paper were those used by the attending roentgenologists of the department and varied with the type of pathology found and the co-operation of the patient. The residents in the department used considerably more time, and thus exposed the patients to larger doses of radiation. The exposures used by these men in the early months of their training period were usually approximately double those employed on similar cases by experienced roentgenologists. On several occasions fluoroscopic exposures used by physicians other than roentgenologists were timed without their knowledge. These were found to be longer than those used by the untrained resident.

So far we have failed to mention the effect of radiation upon the physician or his assistant, or on nurse, friend, or relative, who may be standing near the patient under examination. The radiation which passes through the patient and reaches the fluoroscopic screen is in the neighborhood of 1 per cent of the amount reaching the skin at the point nearest the tube. If the minimum safe daily tolerance dose to skin is considered to be one-tenth of a roentgen per day, only 10 r can be safely administered to the skin of the patient while the unprotected hand of the examiner is exposed. Protection to the hands of the fluoroscopist, therefore, must be conceded to be imperative to prevent destructive skin changes. The amount of radiation reaching the observer through unprotected hand contact is, however, not as important as that reaching the body of the observer and originating in the body of the patient under examination—in other words, the secondary radiation. The exact measurement of these secondary radiation doses is subject to very wide variation due to differences in apparatus and in methods of handling the apparatus, the size of the opening used, the distance between the screen and the patient, etc. It is obvious that the non-radiological specialist, who does not understand the means by which this radiation can be produced, is likely to be exposed to much larger amounts; and naturally if he does not wear a lead-impregnated apron, his body, and particularly the lower portion of his body, will receive an amount of radiation which, accumulated over a period of years, is certainly unsafe.

Braestrup has estimated photographically the secondary radiation reaching the operator, particularly in examinations with horizontal fluoroscopes. Where these instruments are used, the distance between the x-ray cone and the table top is increased in order to allow for movement of the Bucky diaphragm, and a considerable amount of secondary radiation originating in the table top and in the patient may thus pass below the table to the operator. The amount of secondary radiation, according to Braestrup, from below the table top is greater than that originating above. Adequate protection from such radiation can be obtained by the use of lead-impregnated apron and gloves.

In conclusion, it is obvious that fluoroscopic examinations should not be promiscuously done, nor should radiographic examinations be unnecessarily performed where the ovaries or testes of a patient in the reproductive age are to be included in the field. When fluoroscopy is done, some type of limit timer should be used to keep the exposures well within safe bounds, and every fluoroscope should be calibrated as to its x-ray output so that at least the approximate dosage administered can be estimated. The size of the area exposed should be kept to a minimum, and the num-

ber of films made should also be kept down to the lowest number consistent with satisfactory diagnosis. Finally, those who are using the fluoroscope, or who must stand close to the patient undergoing fluoroscopy or radiography, should always wear a protective apron and gloves, keeping the protective lead between themselves and the origin of the ray.

It is not the purpose of this discussion to show that all fluoroscopic examinations are dangerous, and it is almost impossible at this time for one to prove that there is any danger to man even in long fluoroscopic exposures. It is our purpose, however, to draw attention to the fact that very considerable doses of radiation are administered to the patient incident to fluoroscopic and radiographic examinations, and that there are at least potential dangers to the patient, to the operator, and to their offspring, particularly if extreme care is not exercised.

We believe that at the present time, when more and more radiographic and fluoroscopic work is being done by nonradiologists, the attendant dangers must be brought forcibly to their attention.

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Osteogenesis Imperfecta[1]

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ARMAND, IN 1716, reported a case of brittle bones of a newborn infant. This is said to be the first recorded observation of this condition. By the middle of the eighteenth century 30 such cases had appeared in the literature. In 1788 Eckman described a case of hereditary fragility of bones and traced the occurrence of this disease in three generations. Lobstein, in 1833, described the condition as idiopathic osteopsathyrosis or an idiopathic type of bone fragility. Vrolik described brittle bones in 1849 and renamed the condition "osteogenesis imperfecta."

Spurway in 1896 observed a peculiar bluish color of the sclera in association with brittle bones. A more detailed observation concerning the association of these two findings was made by Eddowes in 1900, when he suggested that "the transparency of the sclerotics indicates a want of the quality or quantity of the fibrous tissue forming the framework of the various organs of the body and probably explains the want of spring or toughness in the bones of these peculiar individuals."

Hereditary deafness was reported in 1912 by Adair-Dighton but van der Hoeve and de Kleyn did not observe its simultaneous occurrence with brittle bones and blue sclera until 1916.

Since these cardinal symptoms were discovered and connected, numerous isolated cases and series of cases have been reported in the literature. The clinical picture has been studied and much laboratory investigation has been carried out in an effort to solve the riddle of this disease. A limited amount of pathologic material has been reviewed. Although most authors agree on the observed facts, conclusions concerning the etiology vary, and many physicians are still basing their treatment on unproved hypotheses concerning the true etiologic factor.

TERMINOLOGY AND CLASSIFICATION USED IN PREVIOUS REPORTS

As knowledge of this disease increased, many different names were applied to it. Lobstein's disease (*maladie de Lobstein*) or, as he called it, idiopathic osteopsathyrosis, was first renamed osteogenesis imperfecta by Vrolik. Since that time it has had many other names: fragilitas ossium (Klebs and Hochsinger), brittle bones, blue sclera and otosclerosis (Eddowes's syndrome), osteitis parenchymatosa chronica, dystrophia periostalis, periosteal aplasia, and periosteal dysplasia, have all been applied to one form or another of this disease.

Classifications have been based on the time of appearance of the symptoms, as follows: (1) fetal cases; (2) infantile cases; (3) adolescent cases; (4) late cases.

In the classification which probably is used most widely, the cases of brittle bones are divided into two groups: (1) the hereditary type, which is called an hereditary hypoplasia of the mesenchyme with brittle bones and blue sclera, and (2) the nonhereditary congenital type, which consists of two groups, osteogenesis imperfecta congenita and osteogenesis imperfecta tarda. Blue sclera is considered requisite for the first group, whereas it may or may not be present in the second group.

Similar conditions have been designated by many different names by various au-

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thors. Some authors called cases within the same family osteogenesis imperfecta if they occurred early and osteopsathyrosis if they occurred later in life. Lovett and Nichols called the condition in a parent osteopsathyrosis and in a child osteogenesis imperfecta. This differentiation appears to be much too fine for a condition which presents such uniform clinical and histologic pictures.

ETIOLOGIC FACTORS

The cause of osteogenesis imperfecta remains in the realm of speculation. Many theories have been postulated, though few of them are more conclusive than the original postulation of Eddowes in 1900.

Knaggs has stated that there is an evolutionary failure of the osteoblasts. He thought the basis of this change was either a quality implanted in the connective tissue itself early in development or some outside influence exerted on the connective tissue during development. Key and others have attributed all of the changes to heredity, but they have failed to include the clinically similar group which has no hereditary factor.

The endocrine glands have been implicated by some authors, but the evidence that these structures are at fault is not conclusive. Lack of the enzyme phosphatase and phosphoric esters in the blood, associated with alterations in permeability of the membranes, has been thought by some to be a causative factor.

The fault more likely lies in some inherent defect in the germ plasm, either hereditary or non-hereditary, which does not allow the mesenchymal tissue to develop normally.

MATERIAL STUDIED; CLASSIFICATION AND TERMS USED

This study is based on 40 cases of osteogenesis imperfecta encountered at the Mayo Clinic during the twenty-one-year period 1920 to 1940, inclusive. Because of the multiplicity of names and varied classifications which have appeared in the literature, an attempt has been made to group these cases into a suitable classification which includes all forms of this disease. This is as follows:

Osteogenesis imperfecta.....40 cases
- A. Hereditary type.....11 cases
  (Otosclerosis may occur in any of these sub-groups)
  1. Blue sclera and characteristic roentgenologic changes...3 cases
  2. White sclera and characteristic roentgenologic changes...1 case
  3. Blue sclera and atypical roentgenologic changes.....7 cases
- B. Non-hereditary congenital type .....29 cases
  1. Blue sclera and typical roentgenologic changes.....21 cases
  2. White sclera and typical roentgenologic changes.....8 cases

The term "osteogenesis imperfecta" seems adequate to cover this entire group. Certainly imperfect formation of bone is not limited to any one form of this disease. From the history, the presence of the disease in other members of the same family can be determined. Although clinically it is impossible to distinguish between the hereditary type and the non-hereditary congenital type, it is possible to divide the larger groups into the sub-groups mentioned. We purposely have not used such terms as "osteopsathyrosis congenita," "osteopsathyrosis tarda," and many others found in the literature, since they only contribute further to the confusion concerning this condition.

HEREDITY

Of the 40 cases studied, 11 (27.5 per cent) were of the hereditary type. The most extensive family tree that could be traced led through four generations; brittle bones, blue sclera, and deafness were present in all generations. One patient gave a history of blue sclera in two previous generations of his family, but his own condition consisted only of questionable bone fragility. The defect may be transmitted either by the male or female and follows mendelian characteristics. Once transmis-

sion has begun, no generation is without some stigma of the disease.

The 29 remaining cases (72.5 per cent) were sporadic and no family history of the disease was obtainable.

In the light of our present knowledge, it is impossible to say just when and why this disease procures its hereditary potencies. There seems to be little difference between the manifestations of the hereditary and the non-hereditary types and we wonder if in the sporadic cases the defect may not sometimes be transmitted and thus become the genesis of the hereditary type. Few of the patients who have the non-hereditary congenital type live to a great age and many of them are so badly crippled that they do not marry. Consequently their chances of establishing a family with this defect are greatly decreased. None of the patients who had the non-hereditary congenital type of osteogenesis imperfecta in this series and had reached a marriageable age was married.

AGE AND SEX

The average age of the patients who had the hereditary type of osteogenesis imperfecta when seen at the clinic was thirty years; for those who had the non-hereditary congenital type the average age was 15.2 years when seen. There were 21 males and 19 females.

The most usual presenting complaint was frequent fractures and deformity. Some patients who had the hereditary type of osteogenesis imperfecta came to the clinic for reasons totally unrelated to the skeletal system.

PHYSICAL CHARACTERISTICS

It was impossible to distinguish clinically between the hereditary and the non-hereditary congenital types of osteogenesis imperfecta. The most remarkable finding was the great variation in the severity of the process, from disease in the newborn which was so severe as to be incompatible with life to that in a patient who presented himself because of some unrelated condition and was apparently healthy.

On the whole, these patients were poorly nourished, were short in stature, and presented many deformities. The head tended to assume a triangular shape, with an increase in its transverse diameter. The skull of an infant felt like parchment; the sutures were wide open and there was little real bone. Dentition was frequently poor and the teeth often were soft and carious, with an unusual translucent appearance.

The axial skeleton in the more severe cases was seriously affected. Scoliosis and kyphosis were frequent. In one case, this feature was so severe that the distance between the base of the neck and the sacrum was only 10 to 11 inches (25 to 28 cm.). Deformity of the thoracic cage varied and the ribs and sternum often were twisted and molded to conform to the deviations of the spinal column.

The deformity of the extremities was dependent on the number of fractures and on the success of their treatment. In some cases, the magnitude of the problem of multiple fractures defeats even the best attempts at treatment.

Excessive mobility of joints attributable to unusual laxness of the capsule and ligaments was noted in some cases. These patients are prone to have frequent sprains.

FRACTURES

Multiple fractures occurred in all the cases in our series with one exception. The usual history was that fractures were caused by trauma as slight as rolling over in bed. The pain suffered at the time of fracture was variable, but for the most part was reported to be less than normal. Frequently parents would state that they did not know that their child had sustained a fracture until the deformity had developed. In the entire group of 40 cases 434 fractures were recorded, with an average of 9.2 fractures per case of the hereditary type and of 13.1 fractures per case of the non-hereditary congenital type. The fractures were about equally distributed between the left and the right sides of the body. In order of frequency, the bones most com-

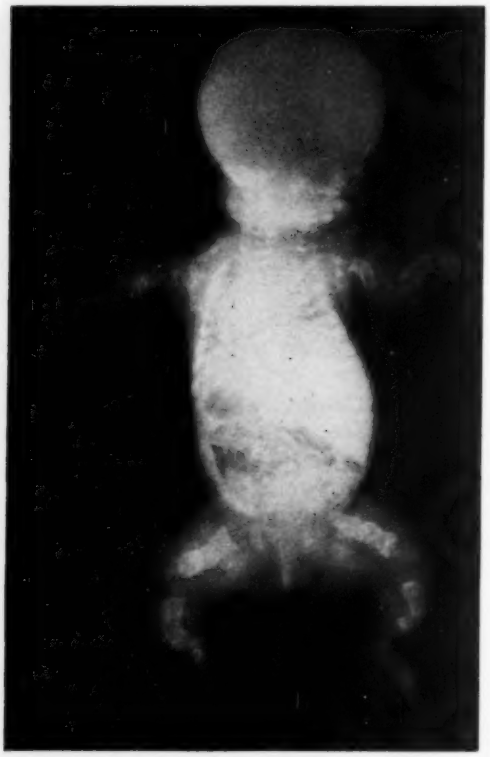


Fig. 1. Entire body of an infant two days of age who died from non-hereditary congenital type of osteogenesis imperfecta. Multiple fractures and pseudofractures of entire skeletal system.

monly affected were the femur, humerus, and tibia. None of the bones was exempt from fractures. The least number of fractures for a patient was one and the greatest number recorded was forty-six. In 7 cases the fractures were too numerous to record.

In cases of the non-hereditary congenital type the fractures occurred earlier, were more frequent, and were caused by trauma of less degree than in cases of the hereditary type of osteogenesis imperfecta.

The fractures were usually of the subperiosteal type with little if any displacement of the ends of the bones but with pronounced angulation at the site of the fracture. Occasionally, oblique fractures were noted, but comminution did not occur in any case. Many incomplete fractures or regions of absorption (Looser zones) were seen in the roentgenograms, and one of us (Camp) believes that the majority of so-called fractures reported in this condition are really pseudofractures or Looser's zones.

The frequency of fractures decreased as puberty was approached and in some cases fractures ceased after puberty.

SCLERA

In the literature there appears to be some doubt as to whether the hereditary type of osteogenesis imperfecta occurs without blue sclera. One patient in this series who gave a history of brittle bones among ancestors for four generations did not have blue sclera. The remaining 10 patients had blue sclera.

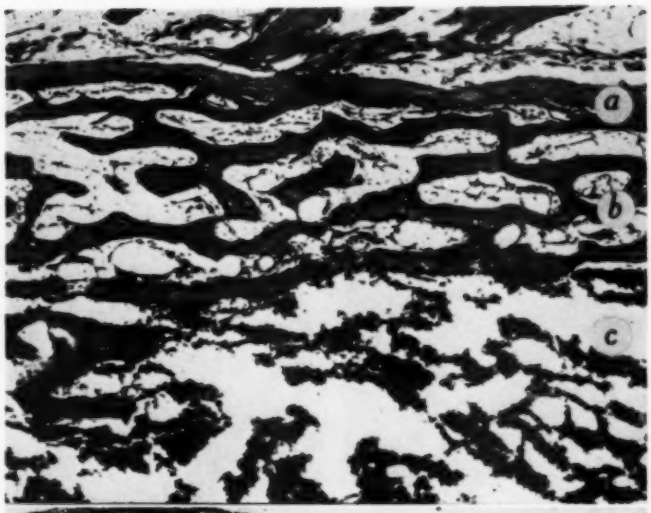
Twenty-one of the 29 patients with the non-hereditary congenital type of disease (72.4 per cent) had blue sclera.

DEAFNESS

Deafness occurred in 5 cases (45.4 per cent) of the hereditary type and in 5 (17.3 per cent) of the non-hereditary type. The higher incidence in the former group can be explained no doubt by the fact that these patients live to a greater age and the otosclerotic type of deafness which occurs in these cases has had time to develop.

LABORATORY FINDINGS

Routine laboratory examinations of the blood and urine gave consistently normal results. Many determinations of calcium, phosphorus, and phosphatase were made on the blood in the cases of osteogenesis imperfecta. The concentration of calcium ranged between 11.4 and 8.9 mg. per 100 c.c. of serum, with an average of 10.12 mg. These determinations were well within normal limits. The concentration of phosphorus ranged between 2.0 and 5.5 mg. per 100 c.c. of serum, with an average value of 4.0 mg. This, too, was normal. The values for phosphatase, as determined in Bodansky units, ranged from 12.9 to 1.8 and, when a division was made into age groups, fell into the normal ranges as determined by Bodansky.



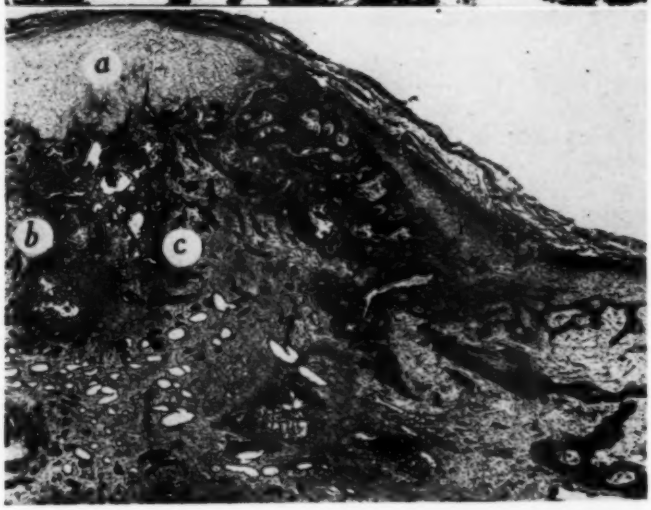


Fig. 2 (above). Cortical bone from infant shown in Fig. 1. *a*. Somewhat thickened periosteum. *b*. Long, slender, loosely interlacing trabeculae with sparse intertrabecular substance. *c*. Rather atrophic marrow substance. ×90.

Fig. 3 (below). Site of fracture in same child, showing an apparently normal reparative process. *a*. Osteoid tissue beneath periosteum. *b*. Necrotic bone and amorphous débris. *c*. Infiltrating blood vessels. ×25.

HISTOLOGIC STUDIES

It was possible to obtain tissue for histologic study in only one of the cases included in this study. The case was that of a newborn child with the non-hereditary congenital type of osteogenesis imperfecta who died two days after birth (Fig. 1). Postmortem examination was made and sections of nearly all the organs in the body were obtained. Unfortunately it was impossible to find any parathyroid tissue, and this gland was therefore not studied. Sections of the thyroid, suprarenal, and thymic glands were normal in all respects. Sections from the pancreas, liver, spleen, and kidney did not reveal any abnormalities.

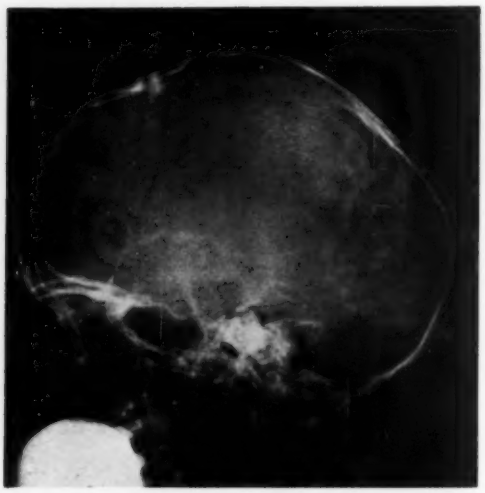


Fig. 4. Skull of a child thirteen years of age, revealing irregular formation and calcification of the cranial bones. Numerous wormian bones are evident about the lambdoid and temporal sutures.

Our observations on the tissue from the skeletal system coincide with those made by Knaggs and Weber in their studies of this condition. The periosteum was somewhat thicker than normal and in many places the trabeculae of the subperiosteal layer of bone were thin or entirely lacking. The trabeculae in the cortical layer of bone were long and slender, and formed a loose interlacing network with the long axis parallel to the long axis of the bone (Fig. 2). The trabeculae themselves were studded with numerous osteocytes, making them more porous than normally. The intercellular substance, as mentioned by Weber, did not stain with a homogeneous color, but appeared blotchy, as though the deposition of calcium had been abnormal.

The osteoblastic fringing of the trabeculae in some areas appeared normal; more frequently these osteoblasts were lacking or had the appearance of dormant cells, often appearing flat and covering the trabeculae much as endothelium lines a blood vessel. Fewer osteoclasts were present than in normal bone.

In the long bones and ribs it was possible to study the sites of previous fractures in various stages of degeneration and repair. The gap was filled with amorphous tissue within which could be detected portions of dead bone and large numbers of multinuclear phagocytic cells. Invading the amorphous regions from each side was vascular reparative tissue with large blood vessels. Beneath the periosteum at each side of the fracture were zones of cellular osteoid tissue in the process of healing the fracture (Fig. 3).

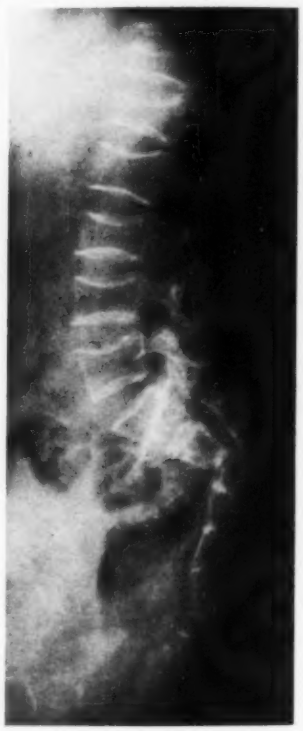


Fig. 5. Lateral view of spinal column of a girl fifteen years old who had the hereditary type of osteogenesis imperfecta. Osteoporosis, wedging of vertebrae, ballooning of intervertebral disks, and angulated fracture of the sacrum may be noted.

On studying the endochondral line of ossification the layer of cartilage cell columns appeared fairly normal. Below this the layer of vesicular cartilage cells was somewhat more loosely arranged than normal. Into the poorly calcified interstitial zone below this, the embryonic bone

marrow and blood vessels were penetrating and eroding in a rather irregular manner. Osteoclasts were not as abundant as would be expected in this region. The embryonic islands of newly forming bone in the subchondral region were widely separated and did not have the normal number of active osteoblasts around their edges.

Fig. 6. Typical picture of hereditary type of osteogenesis imperfecta (same case as Fig. 5). *a*. Pseudofracture of the tibia in the lateral view. *b*. Pseudofracture of the fibula in the area of bowing.

ROENTGEN FINDINGS

Skull: As a rule the skull yielded a typical roentgen picture which was fairly diagnostic of osteogenesis imperfecta. In the early and severe cases the bones which have an anatomically thin cortex were not dense. The bone visible appears to be made up of isolated islands. Early in the course of the disease the suture lines were difficult to discern, but later they were marked by the development of numerous wormian bones especially about the lambdoid and coronal sutures (Fig. 4). An increase in the bitemporal diameter of the skull with decrease in its height was common and in two cases secondary platybasia was noted.

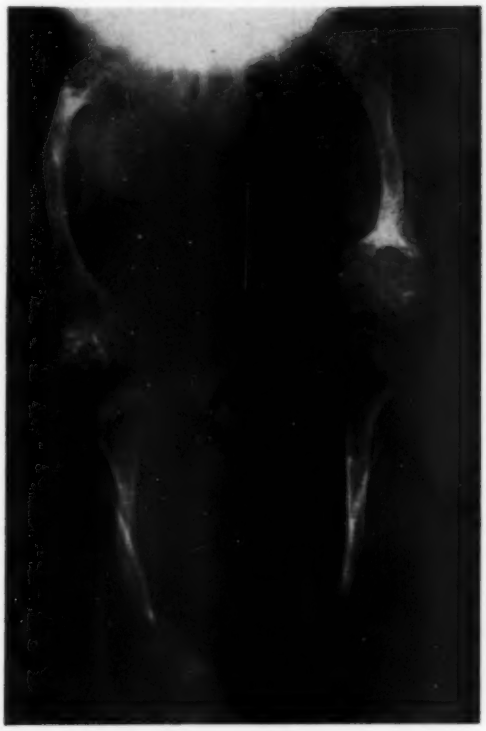


Fig. 7. Clubbing of the diaphyseal ends of the bones with deformed, foamy appearing epiphysis, in patient fourteen years of age who had non-hereditary congenital type of osteogenesis imperfecta.

Vertebral Column: Numerous examples of softening of the vertebrae were seen, with flattening and wedging of the bodies and associated ballooning of the intervertebral disks. One angulated fracture of the sacrum was encountered (Fig. 5).

Long Bones: The characteristic roentgen findings in long bones were a thin porotic cortex and a relatively large medullary cavity (Fig. 6). The cortex was composed of coarse, longitudinally laminated layers which could be seen clearly in the original roentgenograms. This finding was substantiated histologically. The porosis of the bones of the lower extremities appeared to be more severe than that in the upper extremities. This could be explained as an atrophy of disuse subsequent to many fractures and superimposed on al-

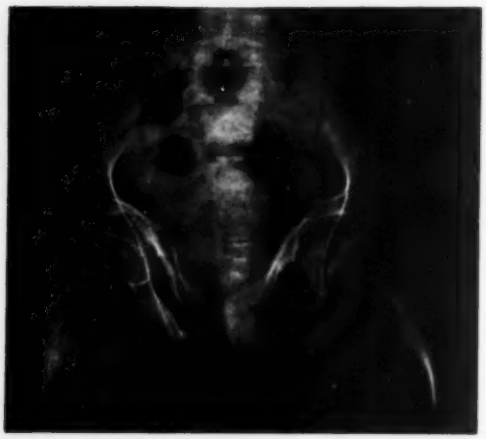


Fig. 8. Rachitic type of pelvis and ballooning of the intervertebral disks with narrowing of vertebral bodies.

ready porotic bone. Small long bones, such as the fibula and ribs, sometimes appeared in the roentgenogram as mere whip-like wisps of bone.

The epiphyseal lines were usually fairly regular and the epiphysis was normal in contour but large in proportion to the size of the diaphysis; in several cases, however, in this series both were grossly distorted and irregular (Fig. 7). In these cases the condition was exceptionally severe and the changes might be interpreted as the result of weight-bearing or trauma to markedly affected epiphyses. Many epiphyses presented a foamy appearance, as if a wildly misdirected attempt had been made to produce normal bony trabeculations. Abnormally early closure of the lower humeral epiphysis was observed in 2 cases.

Bowing and angulation of the shafts of the long bones is the rule. This in many cases was due to the malunion of true fractures. In many bones, however, marked bowing without any roentgen evidence of previous fractures was found. In still other cases there was severe bowing with a pseudofracture (Looser zone) at the apex of the bow.

Other Observations: In 4 cases in this study a rachitic type of flat pelvis was seen (Fig. 8); this with the flattening of the vertebrae leads us to believe that the bones in osteogenesis imperfecta are somewhat plastic when subjected to strains. True fractures or pseudofractures (Looser's zones) may occur in these regions of stress. Definite Looser's zones were observed in 4 patients, and in many cases nearly healed transverse subperiosteal fractures were noted which may originally have been Looser's zones (Fig. 9). Pseudofractures (Looser's zones) may occur in bones without bowing and have been noted to be bilaterally symmetrical (Camp).

In 7 cases of the hereditary type of osteogenesis imperfecta the roentgen findings were not typical of the disease. Because of the history, these cases cannot be excluded. The average age of the 7 patients when seen at the clinic was forty-three years; the youngest was thirty-two years and the oldest fifty-four years of age. The fact that these patients had lived to this age might mean that the process had been milder or that with advancing age the bone structure had become more nearly normal. Roentgenograms revealed normal or slightly osteoporotic bone. In 2 of these cases osteoporosis, scoliosis, and hypertrophic changes in the spine were seen. Unfortunately, routine roentgenograms of the long bones were not made in every instance.

In 4 cases of the hereditary type the roentgen findings could not be distinguished from those in cases of the non-hereditary congenital type of osteogenesis imperfecta. The average age of these 4 patients when roentgenograms were taken was eight years. They did not have the most severe form of the disease and perhaps, as they grow older, their bones, too, will assume a more normal appearance.

TREATMENT

The only specific therapy which has been tried in any of the cases of osteogenesis imperfecta in this series was the subcutaneous injection of thymic extract as prepared by Hansen. This was given to 6 patients, but the subsequent course was known in only 4 of these. An evaluation of the response to treatment is difficult, since the frequency of fractures in untreated

cases is variable. In no case did any startling improvement occur which could be attributed, without doubt, to the extract.

Other measures prescribed were of a general nature to facilitate the absorption and utilization of calcium and phosphorus. These consisted of a diet high in vitamin and calcium, cod-liver oil, calcium given by mouth, and tonics.

Braces and casts were applied in some cases in an effort to prevent and correct deformity. Operative treatment was given a trial in only 3 instances. One patient had undergone four operations for an ununited fracture of the femur with resultant absorption of nearly the entire upper third of the femur. A second patient had multiple bone grafts for ununited fractures of the femurs before obtaining union in one. One autogenous and three homogenous grafts were used. This patient recently had an amputation for the fracture of the united femur. A third patient had a good result following the insertion of a wire for an ununited fracture of the olecranon process.

Many endocrine and hormone preparations have been tried by various authors but none has met with conclusive success.

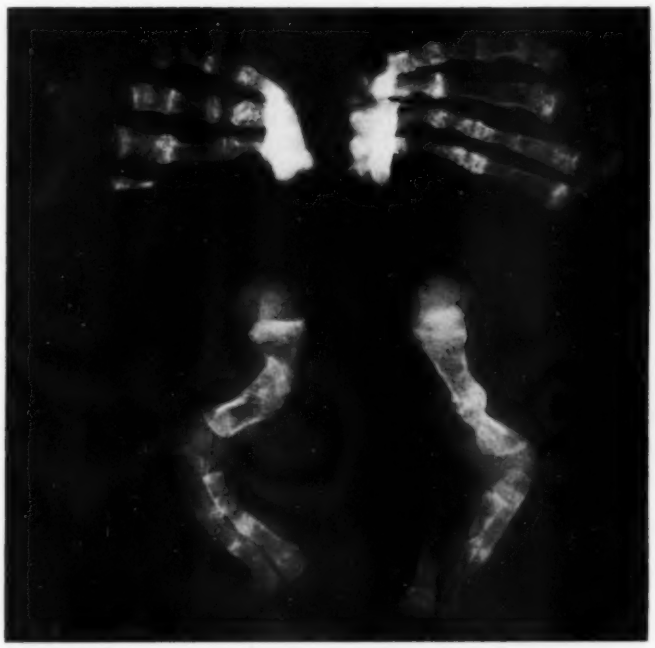


Fig. 9. Necropsy specimens of the ribs and forearms of a two-day-old infant dying from osteogenesis imperfecta. Multiple healed, healing, and fresh fractures of the pseudofracture type may be seen.

COMMENT

Osteogenesis imperfecta is a disease in which the etiologic factor is probably some inherent defect in the germ plasm, which may be hereditary or sporadic. Osteogenesis imperfecta results in maldevelopment of mesenchymal tissues of the body, which is manifest in the main by brittle bones, blue sclera, and osteosclerosis. There is no known specific treatment.

Mayo Foundation
Rochester, Minn.

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Osteopetrosis (Albers-Schönberg Disease), with Case Report[1]

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THE FOLLOWING case of osteopetrosis, or Albers-Schönberg disease, is believed to be the 120th to be reported in the literature.

A nine-year-old boy, complaining that his face was "crooked," was seen by Dr. O. L. Seabaugh, who referred the case to the roentgen department of St. Francis Hospital (Cape Girardeau, Mo.) for examination and courteously permits this report.

In December 1939, the patient had fallen, striking his occiput on the frozen ground. He did not lose consciousness, but was unable, immediately after the accident, to close his left eye and it was noticed that the left side of his face was immobile. Under "electric treatment" this condition was said to have disappeared. Three months before he came for examination, the right side of the face gradually became flaccid, and the appearance was typical of a seventh nerve paralysis.

The boy had had a large head at birth. There was a history of a difficult forceps delivery and resuscitation only after prolonged effort. For two weeks the child lay limp, yet unable to sleep, and had to be fed with a medicine dropper. Subsequently he was bottle fed, receiving in addition cod-liver oil and orange juice. He had three teeth at threee months and the remainder appeared "in order." He walked at eighteen months but until the age of seven his gait was stiff and awkward. During an acute illness in his fifth year his face had appeared "drawn" for a few days. Though he had experienced a number of serious falls, he had never broken any bones. He had entered school at the age of six and had kept up with his classes.

The parents were unrelated. A two-year-old brother was healthy. The maternal grandmother, a great-aunt, and the paternal great-grandfather had carcinoma. The maternal grandfather had tuberculosis, and there was a history of tuberculosis, also, in the father's family. A maternal aunt, now aged 38, had experienced a severe head injury and meningitis in childhood. She was deformed and feeble-minded, and had been told by a physician that her bones were "too soft."

The boy was small—much smaller than a friend of the same age who accompanied him—and pale. He weighed 82 pounds and was 54 1/2 inches tall, well nourished, and fairly well developed muscularly. His head appeared disproportionately large in relation to his body. It was oval in shape, measuring 20.5 cm. in the occipito-frontal diameter and 15.5 cm. bitemporally. The hands and feet were very small. The abdomen was slightly protuberant.

The patient had a ravenous appetite but did not complain of excessive thirst. He recognized neither salt nor sugar on the right side of the tongue. He vomited at irregular intervals without relation to food, the vomitus consisting of a thick mucus. The physical findings referable to the oral cavity and digestive tract were otherwise normal. The spleen, liver, and kidneys were not palpable; there were no abdominal masses, nor did the circulatory, genitourinary, or lymphatic system show any significant abnormalities. Mouth breathing was observed and there were frequent post-nasal clearing noises. There was no thyroid or parathyroid enlargement.

The right side of the face was smooth and immobile, the upper lid could not be closed, and taste on the right side was impaired, as mentioned above. Otherwise the general neurologic findings were not unusual. The patient responded to questioning intelligently and co-operatively. There was no rigidity of the neck, gait was normal, pupils were equal, and response to light and accommodation unimpaired. The tendon reflexes were normal, though rather small in amplitude. The grip was weak in both hands and the boy frequently dropped things.

The eye grounds were normal; the sclerae white.

The patient wore an audiphone on the left side, without which he was totally deaf. The report on the ear condition was made by Dr. M. H. Shelby. At the age of three and a half years there had been a bilateral middle ear abscess, which continued to drain for about six months, when tonsils and adenoids were removed. This operation seemed to clear up the ear trouble, for there was no drainage for about one year. The patient then contracted a "head cold," which was followed by a right otitis media. After a second adenoid removal, the right ear ceased draining within eight to ten days and to the parents' knowledge neither ear had drained since. Hearing had gradually grown worse since the first abscess formation at three and one half years. Examination revealed narrowing of the auditory canals with marked scar formation of both drum heads, so much so that landmarks were obscure. Perforation was not evident on either side. There was now no evidence of drainage from either ear. Hearing tests revealed bilateral conduction and nerve deafness.

In February 1941, when the patient had been treated for acute rhinitis, he was unable to breathe through either nostril. On account of the obstruction to the nares, nasal diphtheria was suspected, but cultures were negative for diphtheria organisms. The obstruction was due more to bony thickening than swelling of the soft tissues.

[1] Accepted for publication in September 1942.

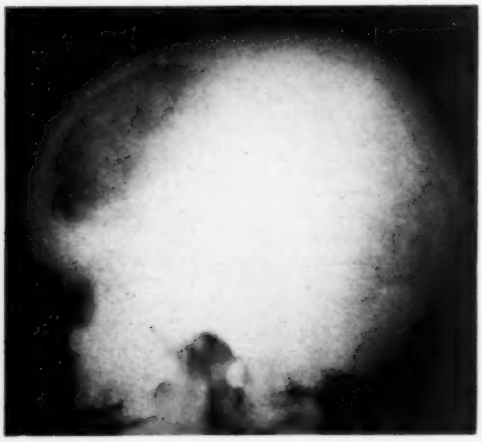

Fig. 1. Lateral view of the skull, showing generalized density with radiolucence in frontal and occipital areas.

The findings on urinalysis were not significant. Blood studies showed: hemoglobin 75 per cent; color index 1; red cells 3,570,000; white cells 5,500; non-protein nitrogen 3.3 mg. per 100 c.c.; sugar 60 mg. per 100 c.c.; calcium 12 mg. per 100 c.c.; inorganic phosphates 5.2 mg. per 100 c.c.; cholesterol 237 mg. per 100 c.c. The basal metabolism rate was −6.

Roentgen studies showed abnormal bone structure throughout the skeleton. A routine lateral view of the skull is reproduced in Figure 1. Except for a portion of the frontal and occipital region the entire skull, including the facial bones, shows a uniform density, quite impenetrable to the x-ray and devoid of normal structural markings. The sella turcica is small, with thick posterior clinoid processes. Buds of unerupted teeth are seen. The frontal and occipital area are so in contrast to the remainder of the skull that at first glance an aerocele is suggested. Here blood vessel markings appear as fine lines. Suture markings are not recognizable. None of the usual air-containing structures is pneumatized. The mastoids do not stand out. The general density involves the nasal bones which encroach upon the nasal spaces. Several cervical vertebrae included in the film are seen to be dense and structureless. Intervertebral discs are unrecognizable except as dense structures fusing with the bodies.

Figure 2 is a view of the same anatomical area taken with greatly increased kilovoltage. The lambdoid and coronal sutures are faintly visible, as are numerous blood vessel markings, usually finer than normal, and convolutional impressions. In the cervical spine the intervertebral disc spaces are recognized.

Figure 3 shows the same structureless density in the ribs, the thoracic and lumbar vertebrae, the pelvis, and the upper extremities of the femurs. In the necks of the latter the bone structure is faintly visible. The ilio-sacral synchrondroses are faintly outlined. Intervertebral spaces are seen in the lumbar region. Of the soft structures, the psoas muscle and kidneys are demonstrable. No renal calculi are present. A lateral view of the spine (Fig. 4) shows the density of the bodies, processes, and laminae

In Figure 5 the lower femurs and upper tibiae and fibulae appear as dense, almost homogeneous structures, with the medullary canal poorly demarcated and no bone detail. The diaphyses of the larger bones show some spreading. The shafts present fine

Fig. 2. Lateral view of skull made at greatly increased kilovoltage, showing convolutional impressions and blood vessel and suture markings.

striations running parallel to the long axes. In the right fibula there is a radiolucent developmental defect at the upper medial border. No calcification of blood vessels or tendons is noted.

Figure 6 shows the right hand of the patient beside the left hand of his friend of approximately the same age. The diaphyses of radius and ulna show a suggestion of structure. The epiphysis of the radius fails to show the articular impress for the navicular and semilunar bones. The small carpal bones correspond to those of a six-year-old child and fail to show normal structure. The rings mentioned by some other authors (8) are not seen. The metacarpals, while dense between the bases and mid-shaft, present a ground-glass appearance of the bases and distal metaphyses. The third and fourth bases are smoothly rounded, presenting no facets for their re-

spective carpals. The epiphyses show faintly normal bone architecture as if through ground glass.

In the proximal phalanges the epiphyses throughout have a ground-glass appearance, as do the shafts in their proximal halves, while the distal halves present a milky white opacity. Normal architecture is absent. The middle and distal phalanges show a similar picture. The entire hand is small and the contrast between it and the normal hand of the other boy is great. Pictures of the patient's foot and the foot of his nine-year-old friend showed the same contrast.

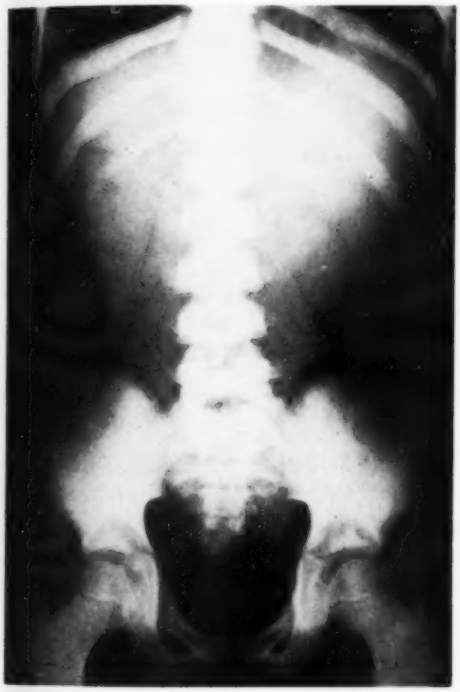

Fig. 3. Ribs, spine, pelvis, and upper femurs. These show the same structureless density as the skull except that in the femurs some architectural detail is evident.

GENERAL DISCUSSION

The case described is a typical instance of Albers-Schönberg disease (osteopetrosis; osteosclerosis fragilis generalisata; congenital osteosclerosis), a condition first described by the physician whose name it bears in 1904 (5) and termed by him "marble bones" because of the density of the skeletal structure. His patient was twenty-six years old and was followed for eleven years, in which time there were no bone changes, though the mental capacity was reduced and the patient had a pronounced pallor. The nature of the condition is no better known today than it was to the discoverer. The number of cases reported, as mentioned above, is small, but well written articles with reviews of the literature are available (1, 2, 12).

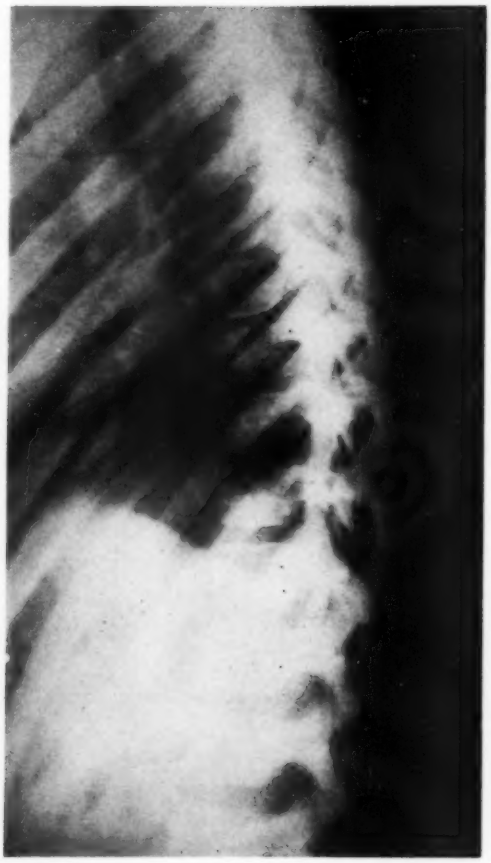

Fig. 4. Lateral view of the spine and ribs; absence of normal architecture.

The signs of the disease are so characteristic that there is no difficulty in making a diagnosis even after an incomplete examination; yet there are many variables. In 2 of the recorded cases the diagnosis was made clinically (2, 14) on the basis of blindness due to optic atrophy, multiple bone fractures, anemia, and stunted growth. In all other instances the diagnosis was made as a result of roentgen studies, either

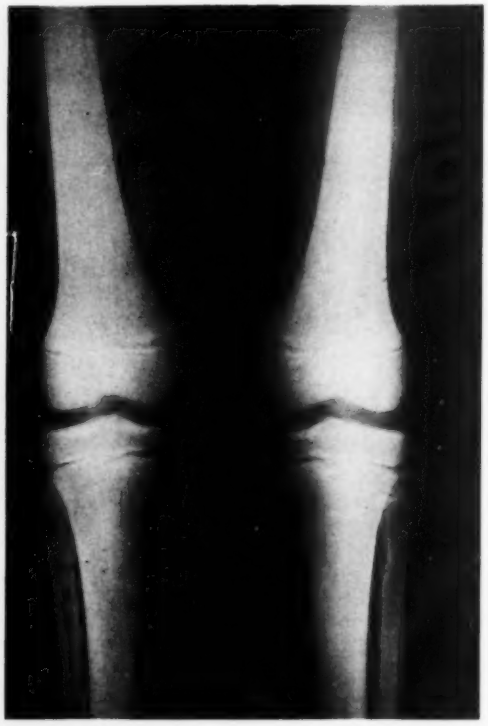

Fig. 5. Lower femurs and upper tibiae. The medullary cavity is poorly demarcated. Longitudinal striations can be seen.

to determine the nature of fractures which had occurred or in search of other conditions. Thus Anthony and Pollack (10), examining a nine-year-old colored girl, blind for seven years, for a fracture of the femur, recognized the abnormality of osteopetrosis on the roentgenogram. They thereupon took films of the optic foramina, which measured 2.4×3 mm. They quote Clegg, who found the normal measurements to be 4.1×4.65 mm., and who concluded that an optic foramen measuring less than 2.8 mm. in any of its diameters could not contain a normal optic nerve. Eye ground examination in this colored girl revealed bilateral optic atrophy. Today the disease should be suspected from the findings and signs mentioned above, especially in children, provided deafness or blindness is present. It is of interest to note that our patient was seen in two large metropolitan hospitals, where the condition escaped detection.

Etiology: It is generally admitted that the cause of the disease is unknown. There are numerous speculations as to its origin. An antenatal process has been mentioned on the basis of the discovery of the disease *in utero* (4, 13), in newborn infants (12), and in young children. We believe that our case began *in utero* because of the large head at birth and the non-aerated cranial sinuses. In support of an antenatal origin Kopylow and Runowa (2) call attention to the absence of pneumatization of the maxillary sinuses, which should take place no later than the fourth month of intrauterine life. They theorize further that, since the other sinuses—frontal, ethmoid, and sphenoid—which should be pneumatized at the age of one and two and one-half years, respectively, are not pneumatized, the disease is a progressive one. McPeak (11) also, in reporting 8 cases, indicates a progression of the disease as age advances. Pirie, who attributes a role to avitaminosis, believes that complete marbling of all the bones does not occur until puberty. Kupylow objects to Pirie's theory of avitaminosis on the ground that in many cases nutrition was not faulty.

The theory of intra-uterine orgin of the disease immediately suggests a possible influence of consanguinity of parents and heredity. Mayer reported a case in the daughter of first cousins (16). Alexander's patient (1) was one of the fourth generation of parents on the mother's side who were cousins. The parents of McCune's patient were cousins, and that author found 6 other such instances in the literature. The parents of our patient were not related.

Pirie (4) records a case in a mother and three childen, while McPeak (11) reports 8 cases occurring in three generations of one family. Hyperostosis of the calvarium, the cause of which is also unknown, was demonstrable in the imbecile aunt of our patient. This case would fit into Moore's (7) classification, which includes hyperostosis fronto-parietalis.

Moore speculates on and then discards the possibility that the endocrine system

is a responsible agent, though obesity is evident in pictures of his patients. The group of glands credited with responsibility of maintaining calcium balance cannot be held responsible, since the pituitary, parathyroids, and thyroid have regularly been found normal when examined postmortem, except that in one instance Pehu, quoted by McCune (12), found an adenoma of the parathyroid gland.

Nature of Lesions: In order to avoid repetition it may be well to consider the gross pathology together with the roentgen findings. The great bone density is immediately demonstrable both roentgenologically and pathologically. A common characteristic of the disease is the occurrence of frequent and multiple bone fractures. This has moved one author (6) to classify the disease under the head of fragilitas ossium. The fractures occur under the slightest insults, such as twisting the body, applying a tourniquet, etc. (For this reason I did not take our patient's blood pressure.) Some heal readily without callus, leaving no evidence (1); others heal with abundant callus; others do not heal at all, and in certain localities, as in the upper ends of the femurs, false joints may be formed (1). Neither Pirie's patient (4) nor ours had any fractures, and fractures

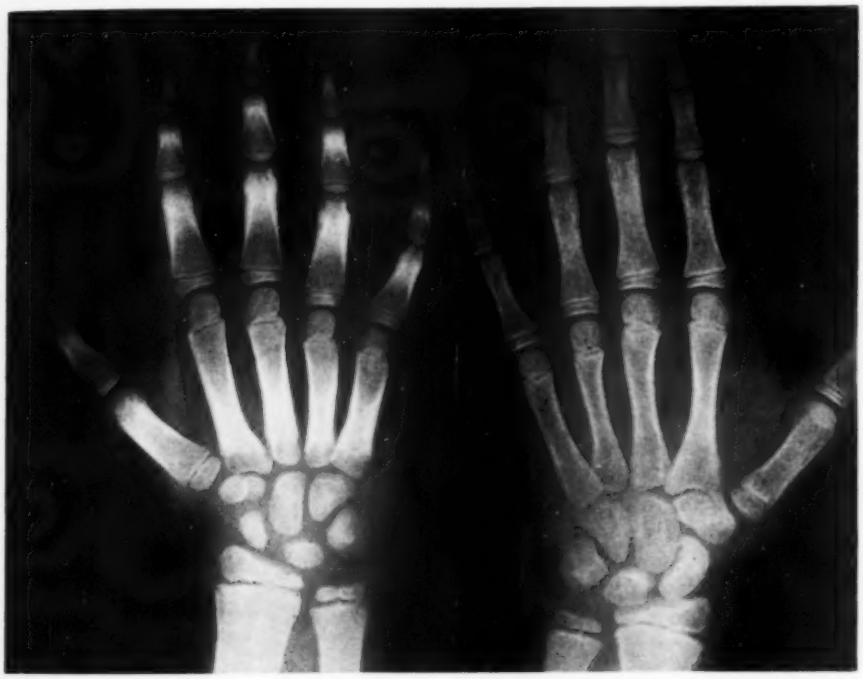

Fig. 6. The patient's right hand, with the left hand of a normal boy of the same age for contrast.

Stressing the hereditary element and frequency of the disease in children, Herscher and Stein (9) favor the theory of a "hereditary defect in the germ plasm carried as a mendelian recessive factor and accentuated by inbreeding." Pirie suggests infection as a cause, and Alexander the existence of a primary rachitic-osteomalacic process.

We believe syphilis, a family history of diabetes, carcinoma, and tuberculosis may be dismissed as etiologic factors on the ground that they are too rarely associated with the disease, though a family history of carcinoma and tuberculosis has been mentioned by some authors and is conspicuous in our case.

were present in only 2 of 8 cases reported by McPeak (11).

In some cases (2), including ours, the general bone contour has been preserved; in others there has been clubbing (1, 10, 11, 12, 14, 15) and again a "fluting" (13) of the long bones. Transverse striations are mentioned in some cases (10, 11). In the case here reported the striations are longitudinal.

The nasal bones deserve more attention than they have received. In our patient these were so thick as to reduce the respiratory lumen and cause frequent post-nasal clearing noises, which probably led to the two operations for adenoids. McCune (12) mentions a nasal discharge and indicates but does not stress the occurrence of thick nasal bones as a cause. Other authors (13) mention nasal discharge and even a typical facial expression (14) but do not anticipate the reasons. Narrowing of the calibre of the auditory meati, as observed in our case, has not been noted, though deafness is mentioned a number of times.

In nearly all cases recorded in the literature available to us the bones of the skull, including the face, presented a homogeneous density. In all cases the base of the skull has been involved In our patient the frontal bones and in Merrill's (3) the facial bones escaped. Retarded dentition with early decay has been observed frequently, and even necrosis of maxilla and mandible has been noted. Our patient had three teeth at three months and when he was seen by us the teeth were in good condition. Vidgoff's patient (8) was born with two teeth. Karshner (14) says the teeth are invariably bad.

Comments on bone density are interesting. Pirie's drill sank into the diseased bone as it would into chalk. At the same time he quotes Henderson as follows: "In the cases operated on the bones are so hard that they break the edge of the chisel or drills." In Alexander's (1) case a nail, intended to secure broken bone fragments, was sheared off. Brailsford (5) examined several bone specimens in the Museum of the Royal College of Surgeons, London, and describes a skull and humerus as ivory hard.

The microscopic descriptions also vary considerably and deserve quoting at some length. Alexander's (1) case came to autopsy and his pathologist, Professor Hart, reports on the bone structure as follows:

"There is a very beautiful picture of new bone formation, as much in the periosteum as in the osteoblasts, which exists as a continuous covering but is composed of low flat cells with dark spindle-shaped nuclei.

"The bony edges everywhere are not only narrow and firm and below the normal breadth, but may be even entirely absent.

"The incomplete new bone picture shows especially in the border between the bones and the cartilages of the ribs and long tubular bones, where the metaphysis shows an entirely undeveloped cortex and a very insufficient spongiosa. In the short bones the entire bone picture is one of generally poorly developed cortex.

"The irregularities of the bone and cartilage zones are dependent for the most part on the deficient activity of the osteoblasts. Osteoblasts were found everywhere, but their number was so small that it constituted real deficiency. Under these conditions, there arises a real complete disappearance of the bone construction.

"A relatively increased content of lime salts, for whose etiology we will need to look further, has thereby appeared in the rapid calcification of the osteoids. The degree of thickening of the bone substance is increased because in the narrow medullary spaces chalk masses have been deposited, which here and there have been found in the narrow blood canals and have completely filled the medullary tissues.

"This deposit of lime is partially found in the walls of the arteries, but is most pronounced in the construction of the medullary tissue.

"This occurs exceptionally in the metaphysis, but for the most part is present in the lymphoid tissue, which, in other places more or less separated, is replaced by a fatty tissue or a very loose tissue composed of an extremely soft fibrous reticulum with small fat cells intermingled."

Describing Kopylow's case (2) Tescherepnina writes:

"The characteristic spongy structure of a piece of excised clavicle with narrow cortex and fine bone columns with wide marrow spaces is replaced by a compact bone mass. In this bone mass the haversian and ground lamellar system are readily recognized. The few marrow spaces contain partly marrow and partly a developing connective tissue.

Most of the spaces are narrowed as a result of thickening of the bony columns. In many areas active osteoblasts and a zone of newly formed bony structure is readily discerned. Occasionally lacunar bone resorption and heaping of giant cells of the osteoclast type is noticed. The entire process presents the characteristics of osteosclerosis in its higher stage of development of eburnation.

"The bone marrow consists principally of myelocytes, stab and juvenile forms, occasional megakaryocytes and normoblasts."

In Pirie's case still other differences are described, namely:

"Section taken so as to include epiphysis, epiphyseo-diaphyseal line and diaphysis presents the following picture: the epiphysis shows relatively normal appearing cancellous bone composed of spicules with very little enclosed cartilage. Between the spicules there is a large amount of relatively hemorrhagic myeloid tissue containing considerable fibrillar matrix. As one approaches the epiphyseo-diaphyseal line there are greater inclusions of cartilage in the bony spicules. The line varies considerably in thickness, showing a firmer, lighter staining, more compact area of cartilage toward the epiphysis and a more cellular cartilaginous zone which varies considerably in thickness toward the diaphysis. The histological structure of the diaphysis is distinctly different from that of the epiphysis. It impresses one as being fundamentally calcified cartilage in which are smaller and larger irregular open spaces. These open areas compose less than 25 per cent of the total structure and are lined by irregular masses of bony tissue. Scattered throughout the calcified cartilaginous material are innumerable small spherical foci of ossification completely surrounded by it so that no open space is present. This arrangement persists well out to the periosteum though there is present a narrow irregular zone of subperiosteal compact bone. Compared with the epiphysis the diaphysis is here much less vascular. The open spaces contain rather cellular, irregular, fibroblastic strands, but few typical myeloid cells. Flattened osteoblasts are conspicuous about the lining of the spaces, but typical osteoclasts are comparatively rare.

"Beyond the end of the bone as one enters the shaft the ossification is much more complete, the open spaces are much larger and myeloid cells are found in them. Even here, nevertheless, there is an abnormal amount of cartilage in the bony spicules and there is a relatively large amount of osteoid tissue. Here a definite zone of compact bone of considerable thickness is present beneath the periosteum."

In Clifton's (13) case no haversian system, canaliculi, or laminae were recognized, nor were there osteoblasts or osteoclasts. McCune and Bradley (12) have summarized the pathological findings of numerous authors.

Aside from bone changes an enlarged liver and spleen have been found a number of times. It has been suggested that this may be a compensatory response (14) to replace the bone marrow hematopoietic function, lost by encroachment of calcium.

Blood chemistry studies are not enlightening, for there is no general departure from the normal. McCune reports slightly low calcium; Kopylow reports a high calcium on one examination, normal in others. The high cholesterol in our case is not explained, nor is the low sugar or increased calcium. Anemia is an associated finding almost without exception and in some cases has reached a severe degree. The explanation seems to lie in the encroachment of calcium on the hematopoietic bone structure. The association of Hodgkin's disease in one case must be looked upon as a coincidence (9).

Some unexpected observations have been recorded. One is that there are no paralyses of spinal nerves, even though the spinal column is extensively involved. One would not expect the pelvic bones to yield normally in response to the requirements of pregnancy and childbirth, yet Alexander's (1) forty-three-year-old patient had six pregnancies with five full-term children.

Prognosis: The answer to the question, "What is to be expected from this disease?" is as has been recorded. The thickened skull bones compress tissues within the cranium as well as structures entering and leaving its orifices and eventually produce hydrocephalus, mental hebetude, headache, vomiting, paralyses of various cranial nerves, which may result in blindness, facial palsy, or deafness as in our case. The poorly developed bones lack elasticity, and break with ease and complications. Encroachment on the marrow brings about blood dyscrasias. Only a few patients have reached an advanced age, and therapy offers no hope. Death is usually due to hydrocephalus, complications following bone injuries, or intercurrent disease.

It is obvious in the light of our present

knowledge that only symptomatic treatment is logical. One author (8) reports improvement from the use of iron.

SUMMARY

A case of osteopetrosis (Albers-Schönberg disease) is reported. The disease is rare and the etiology is unknown. No explanation is offered for this condition in which the unbridled calcium metabolism runs so bizarre a course. The involvement of the nasal bones has been stressed and it has been shown that the auditory meati may be diminished in caliber. A number of variables found clinically, roentgenologically, and pathologically have been mentioned.

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Roentgen Features of Scleroderma and Acrosclerosis[1]

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SCLERODERMA IS not a rare disease. A few cases are seen each year in any large clinic. Likewise, acrosclerosis (Reynaud's phenomenon with scleroderma of the acral parts, face, and neck) is occasionally observed. In 1895 Lewin and Heller (7) collected 507 cases of scleroderma from the literature. Acrosclerosis was first studied and named by Hutchinson (5) in 1893 and was reviewed in 1931 by Sellei (13). Both diseases usually have their onset in early adult life and affect females chiefly. The prognosis in acrosclerosis is said to be better than in scleroderma.

It is the purpose of this communication to bring together the important roentgen features of scleroderma and acrosclerosis. Since scleroderma is a diffuse disease, involving most of the tissues and organs of the body, it is to be expected that the roentgen manifestations will also be diffuse. A considerable thickening and condensation of connective tissue occur. In acrosclerosis there is the added factor of angiospasm. Cases illustrating most of the important roentgen changes will be presented. These changes are: (*a*) calcinosis, (*b*) changes in the osseous system, (*c*) pulmonary fibrosis (questionable), (*d*) esophageal stenosis (occasional).

(*a*) *Calcinosis* is the most striking roentgen feature. Thibierge and Weissenbach (14) collected 9 cases of scleroderma with calcinosis, which had been published up to 1911. Durham (3) reported an additional case and reviewed 13 others between the years 1911 and 1926. Three cases of acrosclerosis were included in this group. Several cases have been reported subsequently. According to Durham, the incidence of calcinosis in scleroderma is 1 in 60. Usually it involves only the areas of skin sclerosis. It is not commonly found beneath normal skin. Scholz (12), however, has reported a case in which the calcium deposits were present beneath normal skin beyond the clinically visible areas of sclerosis. Calcinosis does not appear to be confined to any single type of scleroderma. It involves areas of the body that are subjected to pressure. The finger tips, elbows, and ischial tuberosities are commonly affected. In acrosclerosis, the hard plaques are often palpable, and ulceration of the distal phalanges is the rule. Small particles of calcium may be extruded from these ulcers. Uric acid has not been found in these areas. They are made up of calcium carbonate and calcium phosphate and vary in size from minute dots to large plaques. A significant increase in the blood calcium has not been reported.

(*b*) *Changes in the Osseous System:* A slow progressive absorption of the distal phalanges of the fingers is a common finding. This absorption is seen most commonly in acrosclerosis. The disease has usually been present for several years before marked absorption occurs. An increase in the calcium content of the distal phalanges may also occur. Podkaminsky (11) and also Edeiken (4) believe that the calcinosis, an associated terminal absorption, and an occasional increased intra-osseous deposition of calcium form a characteristic triad and aid in differentiation from other diseases causing absorption of the distal phalanges of the fingers. Synostosis between the distal and middle phalanges may occur. Subluxations have also been reported.

Other bony changes occur but are not frequent and are not characteristic. Association of scleroderma and melorheostosis

[1] From the Department of Roentgenology, Cleveland City Hospital, and The School of Medicine, Western Reserve University. Accepted for publication in September 1942.

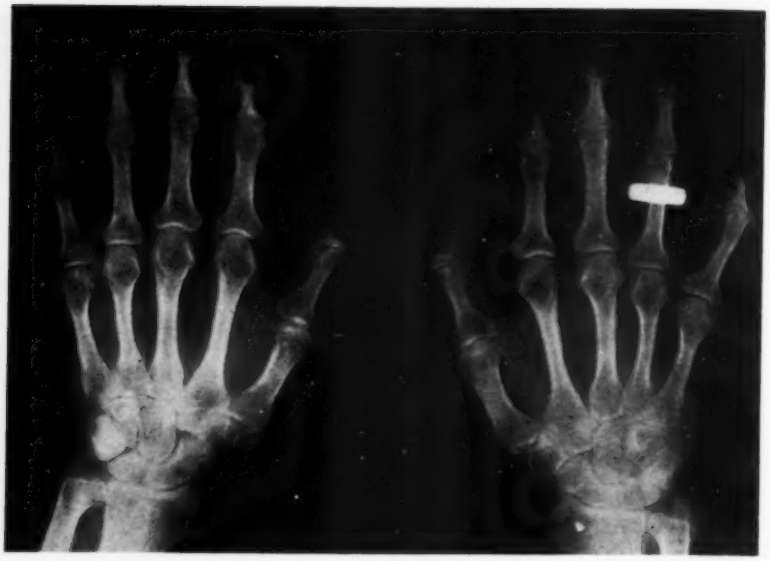


Fig. 1. Case 1: Bilateral absorption of distal phalanges.

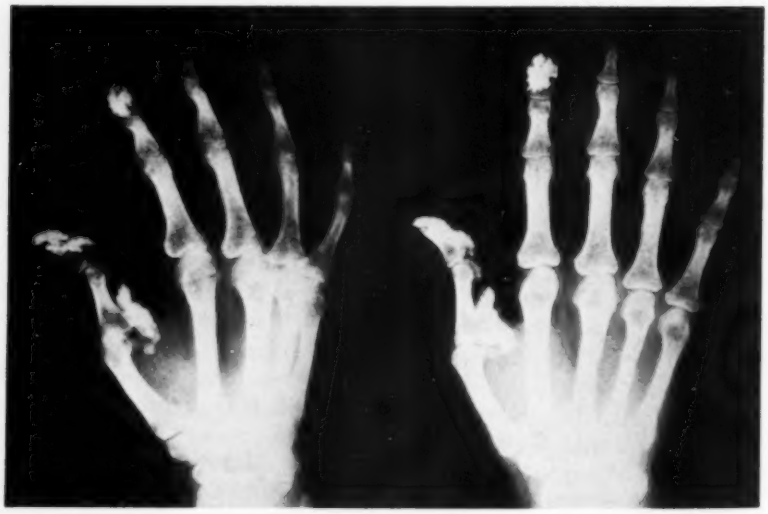


Fig. 2. Case 2: Calcinosis of the base of the thumb and of the index finger. Mutilation of the distal end of the middle finger.

Leri has been reported. Osteoporosis and kyphosis of the spine and enlargement of the sella turcica have all been observed.

(*c*) *Pulmonary Fibrosis:* Two of the cases presented here showed shadows which we interpreted as fibrosis of the lungs. The apparent fibrosis varied from fine to coarse strands and was most prominent in the lower portions of the lungs. The apices are usually spared. A diffuse "characteristic" pulmonary fibrosis has been described at autopsy by Kraus (6). Murphy, Krainin and Gerson (9) have reported a case of scleroderma in

which the fibrosis was said to be visible on a chest roentgenogram.

(*d*) *Esophageal Stenosis:* One of the patients to be described here complained of dysphagia. A barium meal revealed eight-hour retention of barium in the esophagus. The appearance was that usually seen in cardiospasm. Esophagoscopy was not done. Dowling (2) has reported a case in which there was esophageal obstruction on roentgen examination and it was found at autopsy that the esophageal muscles were involved by the scleroderma, thus causing the obstruction.

CASE REPORTS

CASE 1: A 41-year-old white female, born in Greece, was admitted to Cleveland City Hospital April 16, 1936, complaining of pain and deformity of the fingers of both hands. Pain had been present in the fingers for the past ten years. Ulceration had occurred at the tips of the phalanges several years ago and now these phalanges were almost absent. Cold weather caused the hands to turn bluish black.

Examination revealed a macular eruption of the skin of the face, hands, and arms. The lesions varied from 2 to 3 mm. in diameter. There was atrophy of the distal phalanges of the hands. The skin was firm, thick, and inelastic.

In a section of the skin removed from one of the hands for histologic examination, the most striking changes were in the corium, where a profound increase in the dense collagenous connective tissue containing few cells was found.

The Kline test, blood urea nitrogen, basal metabolic rate, and routine blood and urine examinations were all normal or within normal limits. The serum calcium and phosphorus, measured 10.0 and 4.0 mg. per 100 c.c., respectively. Phosphatase measured 7.1 Bodansky units.

Roentgenograms of the hands (Fig. 1) revealed marked absorption of the distal phalanges typical of acrosclerosis. The clinical impression, also, was that the case was a typical acrosclerosis.

CASE 2: A 46-year-old white female, born in Indiana, was admitted to Cleveland City Hospital on Nov. 3, 1941. Her complaints were weakness of the lower extremities, ulceration of the right foot, and stiffness of the hands. The present illness began with coldness in the fingers five years before admission. The fingers had been cold and white at intervals since. Weakness of the legs and an ulcer on the dorsal surface of the right foot had been present for the past seven months. There was a macular eruption on the face, neck, and chest. The nose was thin and pointed. The skin of the finger tips was white and shiny and small ulcers

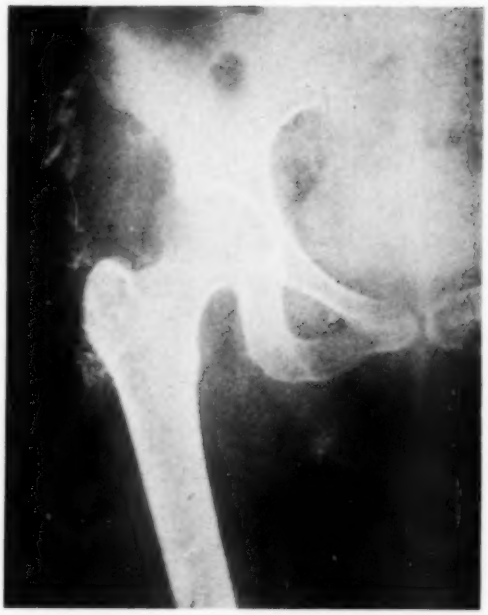


Fig. 3. Case 2: Extensive calcinosis of the thigh and in the region of the ischial tuberosities.

were present on some of the distal phalanges. Hard, bone-like plaques were palpable in the distal end of the right index finger and at the base of the right thumb. Similar plaques could be felt in the region of the ischial tuberosities and in the upper thighs.

Roentgenograms of the hands revealed dense plaques of calcium in the soft tissues of the distal phalanx of the right index finger and at the base of the right thumb (Fig. 2). There was early bone absorption of the distal phalanx of the right middle finger. Calcified plaques were present in the thigh and gluteal regions (Fig. 3). Roentgen examination of the skull, feet, chest, esophagus, stomach, and duodenum revealed no evidence of organic disease of any of these structures.

Histologic examination of a portion of skin and muscle revealed changes consistent with scleroderma. The basal metabolic rate was plus 25, blood cholesterol was 143 mg. per 100 c.c., and blood calcium and phosphorus determinations were normal. The blood Kline test was negative.

The clinical impression was acrosclerosis. The extensive calcinosis in this case is unusual. Further absorption of the terminal phalanges is to be expected.

CASE 3: A 55-year-old white female, born in Russia, a housewife, was admitted to Cleveland City Hospital on July 23, 1940. There had been previous admissions in 1930 and again in 1935. The patient had been well until 1927. At that time she became aware of uncomfortable sensations in her neck and noticed that her skin was becoming thick

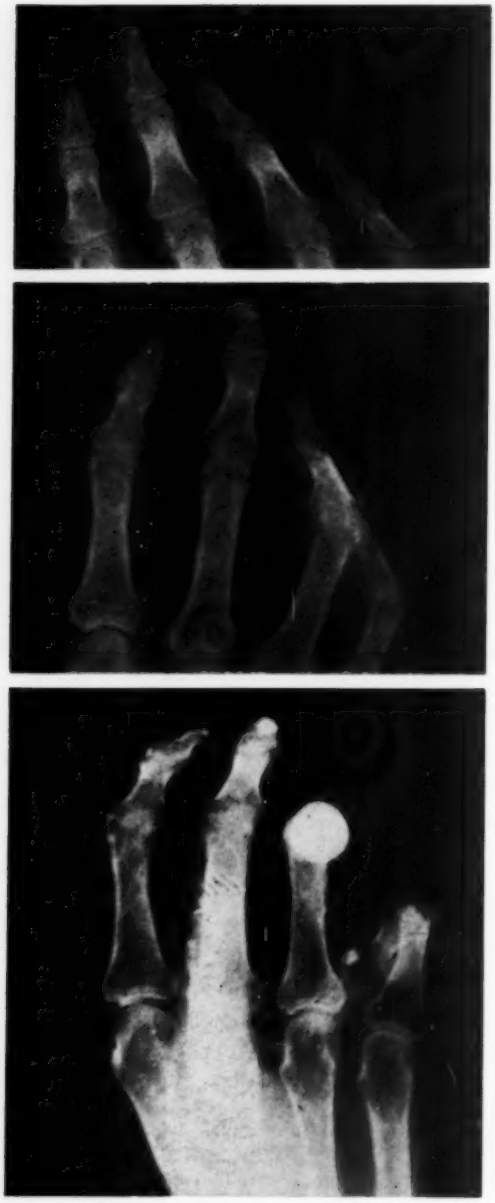


Fig. 4. Case 3: Successive films of right hand, made in 1930, 1935, and 1940 (reading from above down). Note the slowly progressive absorption of the distal end of the middle finger.

and slightly discolored. Adrenalectomy was performed elsewhere for hypertension in 1927. For the past several years the patient had noted the presence of painful ulcers on the tips of the fingers. There was no history of respiratory infections or of pneumonia. For several years, however, there had been a feeling of heaviness in the chest and burning immediately after eating. Vomiting had not occurred.

Physical examination revealed masked facies with thick, shiny, indurated skin. There was limitation of motion of all joints. The heart was enlarged and the blood pressure measured 250/100. Routine blood and urine examinations were negative. The blood calcium was 10.2 and phosphorus 4.2 mg. per 100 c.c.

The clinical impression was scleroderma.

Roentgenograms of the right hand were made in 1930, 1935, and in 1940 (Fig. 4). They show a slowly progressive absorption of the distal phalanx of the middle finger. There was slight calcification of the soft tissues of this phalanx in the last two examinations. Calcium deposits were also present in the region of the left ischial tuberosity (Fig. 5) and around the left elbow. A chest roentgenogram revealed a shadow interpreted as a coarse fibrosis of the left upper and right lower lobes (Fig. 6). It was not possible to determine whether the fibrosis was secondary to the *cardiac disease* or due to the scleroderma, or of some other cause. A barium meal was administered and, although small amounts entered the stomach at intervals, barium was retained in the esophagus eight hours after administration (Fig. 7). Esophagoscopy was not done.

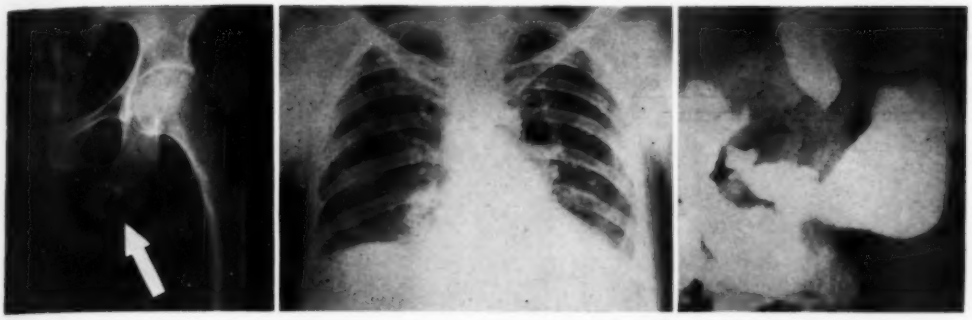
CASE 4: A 46-year-old white female, born in the United States, was admitted to Cleveland City Hospital on May 19, 1941. The chief complaints were painful fingers, thickening of the skin of the fingers and of the face, and loss of 25 pounds in weight during the past six months. There was no history of cough and no gastro-intestinal symptoms were present.

The patient was still obese despite the history of weight loss. The skin of the hands was shiny and inelastic. Examination of the chest and abdomen revealed no abnormalities. Results of laboratory examinations were all normal or within normal limits. The blood calcium and phosphorus were normal.

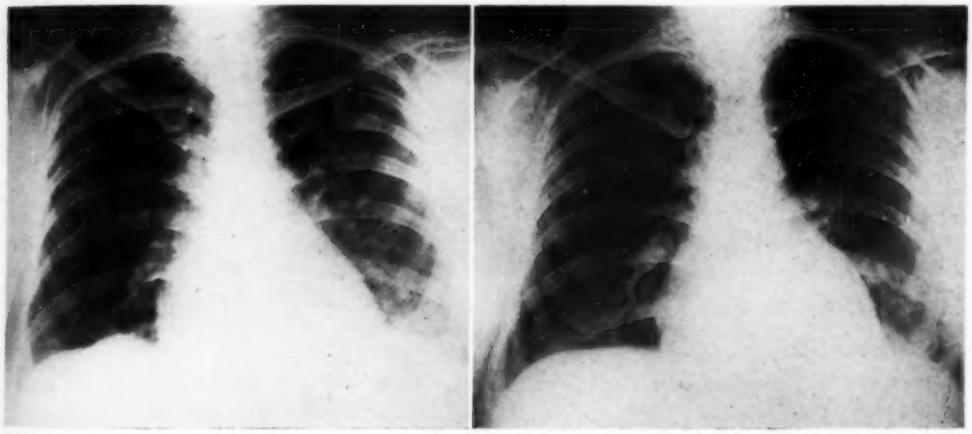
Several roentgen studies of the chest were made. Two of these are reproduced (Figs. 8 and 9). Examination of each film revealed a shadow suggesting fine fibrosis of the lungs, chiefly on the left side. Films of the hands showed no abnormality. The patient was given physiotherapy without benefit. She was discharged ten weeks after admission unimproved.

The patient was bedridden at home and was readmitted on Nov. 2, 1941, with convulsions. She died two hours after admission.

Autopsy, performed by Doctor John Paget, revealed many coarse hyalinized bundles of fibrous connective tissue in the skin. There was hyperplasia of the spleen and lymph nodes. The lungs revealed interstitial and perivascular fibrosis (Fig. 10), probably scleroderma; the distribution was similar to that seen on the films. There was mucosal and submucosal fibrosis of the stomach and colon.



Figs. 5–7. Case 3: Fig. 5 shows calcification near the left ischial tuberosity. Fig. 6 is a chest film made on Aug. 15, 1940, showing the shadows interpreted as fibrosis at the base of the right lung and throughout the left lung. Fig. 7 shows the appearance of the esophagus and stomach shortly after the administration of barium. Barium was retained in the esophagus eight hours after administration.



Figs. 8 and 9. Case 4: Chest roentgenograms showing the shadows that were interpreted as fibrosis of the lung. These are especially prominent at the right base and throughout the left lung. Fig. 9, on the right, shows the persistence of these shadows three weeks after the first film was made.

Severe vascular disease was found in all sections except the brain. The large arteries showed intimal proliferation with occasional cellular infiltration of the intima. The predominant cell was the lymphocyte. The arterial disease was not considered to be polyarteritis nodosa.

COMMENT

The essential pathologic finding in scleroderma is thickening and sclerosis of the collagenous bundles. The disease is not limited, however, to the skin and underlying connective tissue. Muscle, bone, and fascia are said to participate in the pathologic change. This may explain the occurrence of pulmonary fibrosis and esophageal stenosis. The necrosis of the terminal phalanges of the fingers is secondary to the associated vasospastic phenomena which accompany acrosclerosis.

The occurrence of calcinosis may be explained on the basis of the solubility of lime salts in acid and alkaline media. These salts are more soluble in acid media and remain in solution in normal tissues whose carbon dioxide tension is high because of the active metabolism. In dead tissues there is lowering of the carbon dioxide tension as a result of lowered metabolism. The reaction becomes alkaline and lime salts are precipitated from blood and lymph which diffuse into the area (8).

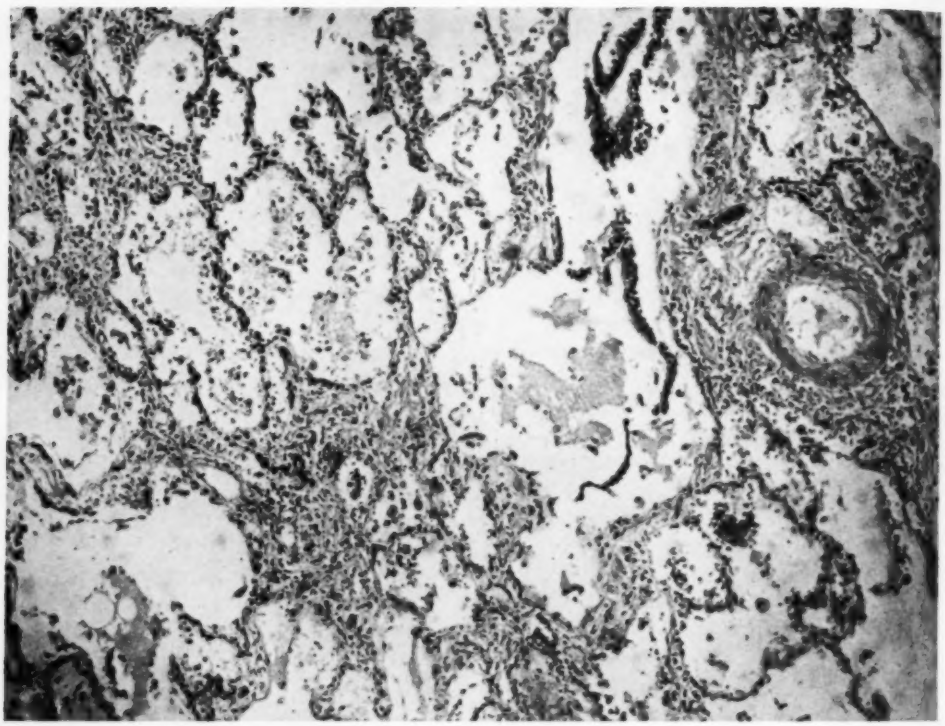


Fig. 10. Case 4: Section from the left lung, showing diffuse pulmonary fibrosis. The fibrosis was widely distributed throughout both lungs.

SUMMARY

On the basis of four cases and a study of the literature, the roentgen features of scleroderma and acrosclerosis have been described. They include absorption of the bones of the terminal phalanges of the fingers, calcinosis, and occasionally pulmonary fibrosis and esophageal stenosis.

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Congenital Atresia of the Esophagus: Report of Four Cases[1]

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CONGENITAL ATRESIA of the esophagus is a rare condition but is probably more often present than diagnosed. The literature offers conflicting statements as to the incidence. The first case of this anomaly was reported by Durston (3) in 1670. Cautley (2) saw one case in twenty-five years of practice, whereas Gage and Ochsner (4) saw 6 cases in fifteen months. Shukowsky and Baron (9) observed one example in 50,000 births, and Lanman (5) in 1940 reported 32 cases which were seen at Children's Hospital of Harvard Medical School over a period of eleven years. Rosenthal (8) collected 255 cases from the literature in 1931; Strong and Cummins (10) brought this number up to 263 in 1934. Several cases have been reported since, but the number recorded still does not exceed 350. We have 4 cases to report, observed within the past three years: 3 from the University Hospital (University of Oklahoma) and 1 from St. Anthony's Hospital of Oklahoma City.

This condition consists in a blind conical ending of a somewhat dilated and hypertrophic esophagus, usually at the level of the fourth cervical vertebra. This is about 34 mm. below the larynx and 12 cm. from the central incisors. The dilatation and hypertrophy are probably due to attempts at swallowing amniotic fluid in intrauterine life. In the majority of the cases the distal part of the esophagus extends as a narrow tube up to the trachea or, rarely, to one of the main bronchi (usually the right), thus establishing a communication between two important systems in the body economy—the digestive and respiratory. This so-called tracheo-esophageal fistula was present in 215 of Rosenthal's 255 collected cases, representing 84 per cent. Rarely is there a fistula between the trachea and the upper segment of the esophagus. The two segments of the esophagus are usually separated by 4 or 5 cm. but may overlap as much as 1.5 cm. There is striated muscle in the upper portion and smooth muscle in the lower or distal segment. The fistulous opening into the trachea frequently looks like the ureteral opening of the bladder.

Other malformations often occur with this anomaly. Of these, imperforate anus and atresia of the rectum have been most frequently observed. Is it not interesting to find at each end of the primitive gut frequently associated anomalies? Horseshoe kidney, unilateral kidney, double uterus, harelip, and hemorrhagic disease of the newborn were also reported as associated conditions. Two of our four patients had hemorrhagic disease of the newborn. It is of interest to note that Plass' (7) series of 94 collected cases, published in 1919, revealed 59 instances of accompanying anomalies, representing 62.5 per cent; 24 of the 59 anomalies were atresia ani. Statistics published more recently show the presence of associated malformations much less frequently than Plass' paper. Probably the wider use of roentgen examination is responsible for the diagnosis of the less obvious cases, which were discovered rarely in the past.

In order to obtain an accurate concept of the anomaly under consideration, a review of the developmental anatomy of the esophagus and trachea is necessary. The esophagus and trachea develop from the foregut, which is the cephalic portion of the primitive gut. The upper and lower halves of the esophagus develop separately. The lower half arises from the pregastric segment of the foregut, while the upper half, or so-called paratracheal portion, and the entire trachea are derived from the retro-

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pharyngeal segment of the foregut as a single tube. This common tube is divided into the anterior trachea and posterior esophagus by the development of external longitudinal grooves, one on each side, which eventually unite to form two separate tubes. The long buds appear on the ventral surface of the anterior tube or trachea (see Fig. 1, Plate 1). All of these

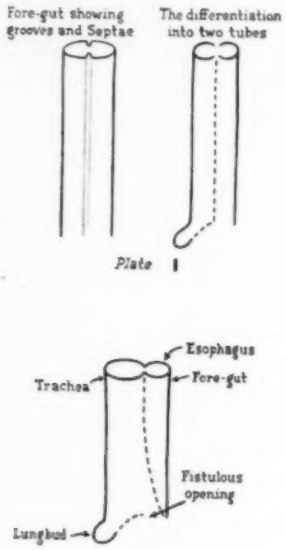

Fig. 1. Plate 1. Normal division of the foregut into trachea and esophagus. Plate 2. Formation of congenital esophageal atresia by diagonal development of the dividing septa and grooves of the foregut.

changes occur in the first seven weeks of intra-uterine life. The anomaly, therefore, is present in the two-month embryo.

In the development of atresia there is an abnormal separation of the foregut. This is more readily understood if one imagines the septa and grooves as developing in a diagonal rather than a longitudinal manner. This is diagrammatically shown in Figure 1, Plate 2. It could also be shown in a diagrammatic sketch of the autopsy specimen of one of our cases.

It is thought-arresting to speculate as to the cause of this radical departure from the normal in this particular stage of development. Numerous theories have been advanced. As with other malformations of development, which are not infrequently associated with esophageal atresia, trauma and intra-uterine inflammation have both received consideration as etiologic factors. Pressure on the yet undivided tracheo-esophageal tube by aberrant blood vessels or by the heart has been suggested among other possibilities. After all theories have been weighed, however, one must exclude the presence of any extrinsic factor and return to the fundamental one, namely, a primary deficiency in the developmental capacities of the corresponding entodermal cells in the tissues concerned. MacKenzie (6) reported this condition in three children of the same father but of three different mothers. His report and the astonishing similarity of the macroscopic pathology of all recorded cases strongly support this theory.

It is natural that the symptoms of this anomaly are strikingly uniform, since the anatomical changes are similar. The one warning sign which may be seen is the overabundance of amniotic fluid at the time of parturition. Whether or not this hydramnion is due to inability of the fetus to swallow amniotic fluid, as Ballantyne (1) has suggested, we are not prepared to say. It seems certain, however, that other anomalies are frequently heralded by the same manifestation. The newborn infant appears of normal weight and cries readily; no abnormality is at first apparent. The first sign which may be noted is a constant drooling of saliva and mucus during sleep. The abdomen is shallow; but in the presence of an accompanying broncho-esophageal fistula, which is observed in about 90 per cent of the cases, the air-filled stomach produces a fullness in the epigastrium in contrast to the shallowness of the lower abdomen. The dramatic event occurs when the baby is first put to the breast. The first few swallows are normal (filling of the proximal segment), but are followed by violent spasmodic coughing with regurgitation of frothy milk and

Fig. 2. Case 1: Upper segment of atresic esophagus filled with lipiodol.

mucus and rapid onset of cyanosis. The child appears literally to drown in its mother's milk. After a rather rapid recovery, the attempt at feeding is again made with a repetition of the results described. There follow enormous distention of the upper gastro-intestinal tract with air, signs of dehydration, as evidenced by the blood examination, depressed fontanelle, meconium stools with no lanugo hairs, only bile-stained mucus, scanty concentrated urine, fever, inanition, and, frequently, aspiration pneumonia.

Obstruction to the passage of a catheter into the esophagus, 12 cm. from the central incisors, strongly suggests the diagnosis. Roentgen examination by contrast media reveals the upper segment of the esophagus as a distended sac ending blindly somewhere above the tracheal bifurcation, most often at the level of the fourth dorsal vertebra. If the stomach containing gas can be demonstrated roentgenographically, this is a diagnostic sign of the presence of tracheo-esophageal fistula. The contrast medium used should be lipiodol and not a barium mixture, since aspiration of the latter may lead to bronchopneumonia. Recently, air injection has been suggested instead of lipiodol.

Confusion in diagnosis most frequently occurs in birth injuries, brain injuries, enlarged thymus, atelectasis, and pneumonia.

Treatment has not been effective as to cure but only for palliation. It consists in a tying off of the cardiac end of the esophagus in order to prevent regurgitation and a gastrostomy for feeding. Theoretically, it should be possible later to form an anterior thoracic esophagus by removing the upper segment to the neck, but no child has survived a sufficient length of time to permit such an attempt.

CASE REPORTS

CASE 1: B. E. J., a two-day-old boy born at term (spontaneous delivery), was brought to the University Hospital with a history of blue discoloration at birth. He had never breathed well and vomited everything over a teaspoonful of nourishment, with accompanying mild attacks of blue discoloration and breathlessness. The family history was unimportant.

The child was well developed but acutely ill. The face was cyanotic, respiration was labored, and mucus was exuding from the mouth and nose. Interspaces showed slight retraction; there were coarse breath sounds, moist râles, and no demonstrable dullness. The heart was essentially normal; no visible peristalsis or palpable abdominal masses were observed. The extremities were essentially negative.

The temperature was 104.6°; respiration 50;

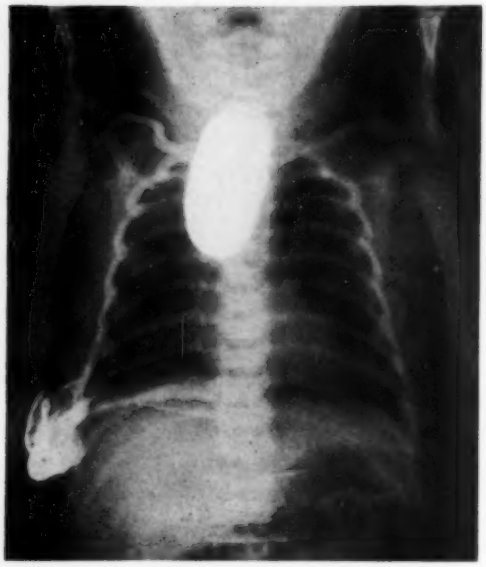

Fig. 3. Case 2: Dilated upper segment of atresic esophagus demonstrated by lipiodol.

hemoglobin 100 per cent; red blood cells 5,720,000; white blood cells 14,900, with 70 per cent neutrophiles. A flat plate of the chest and abdomen revealed no pulmonary pathology; the stomach was distended by gas, and the small bowel contained a moderate amount of gas. Lipiodol injection into the esophagus (Fig. 2) revealed a complete atresia at the level of the fourth dorsal vertebra and moderate distention. Since the gastro-intestinal tract contained gas, a diagnosis of congenital atresia of the esophagus with tracheo-esophageal fistula was made.

A jejunostomy was done on the third day. Air exuded from the intestine on incision and a No. 18 French catheter was inserted into the jejunum. The patient did not respond satisfactorily; cyanosis persisted, the lungs repeatedly filled with bloody fluid, and respiration became rapidly worse. Death occurred three days after admission, sixteen hours after operation.

Autopsy revealed a complete atresia 3 cm. below the glottis. The proximal end of the esophagus was slightly dilated. Immediately distal to the atresia was a thin strand of tissue, approximately 4 mm. in diameter, that contained no lumen. This extended downward for about 2 cm. and was attached to the distal portion of the esophagus, which appeared normal. At this point, there was a fistulous opening of the esophagus into the trachea, approximately 2 cm. above the level of the bifurcation.

The stomach was expanded; the mucosa was thin and smooth. The duodenum was discolored a deep purplish gray and distended with air, as was the jejunum in its proximal two-thirds. Distal to the jejunal incision was complete collapse of the entire small and large bowel. There was evidence of hemorrhage from a mesenteric vessel about the area of the jejunostomy.

CASE 2: M. C. C., a white boy, was born at the University Hospital, weighing 9 pounds, 11.5 ounces. He seemed narcotized for a short period after birth, but responded without stimulation. The infant had persistent mucus in the pharynx, requiring repeated aspiration, and he regurgitated all feedings, with periodic attacks of cyanosis. A diagnosis was made of esophageal stricture or atresia, with the possibility of tracheo-esophageal fistula, and the latter was confirmed by x-ray studies. Physical examination revealed no pathological changes in the abdomen, chest, mouth, or throat. Temperature, pulse, and respiration were normal. The red blood count was 6,380,000; white blood count 11,900, with 61 per cent neutrophiles.

The flat plate of the chest was essentially negative. Lipiodol injection into the esophagus revealed an atresia at the level of the fifth dorsal vertebra and great distention (Fig. 3). Stomach and intestines were moderately distended by gas, suggesting a broncho-esophageal fistula.

On the fourth day a gastrostomy was performed under local anesthesia and a No. 18 catheter was placed in the stomach through a small opening. The patient did not do well after operation and passed bloody stools. A blood transfusion was given but death ensued fifty-two hours after operation.

At autopsy the esophagus was found to terminate in a blind pouch approximately 5 cm. below the pharyngeal end of the esophagus. Immediately below this the esophagus communicated with the trachea by a tracheo-esophageal fistula. From the fistulous opening to the cardiac end of the stomach, the esophagus was patent.

The stomach was filled with dark, unclotted blood. The lungs revealed scattered irregular reddish gray areas. The parenchyma was crepitant and the cut surface retracted slightly. Bronchioles were patent and the mucosa slightly injected throughout. The arteries were patent.

CASE 3: M. A. H., a white girl, was born at St. Anthony's Hospital (spontaneous normal delivery). She weighed 5 pounds 4 ounces and appeared normal at birth. She seemed to nurse normally but vomited mucus and milk and became cyanotic after each feeding. A diagnosis of thymic hypertrophy was made and roentgen therapy was instituted. Roentgen examination showed obstruction of the esophagus at the level of the arch of the aorta (Fig. 4).

At the age of three days a gastrostomy was done without relief. A large amount of gas was expelled through the gastrostomy tube, but regurgitation of milk and cyanosis continued on each attempt at feeding by mouth. The baby died at the age of five days, apparently from pneumonia, forty-eight hours postoperatively. Postmortem examination showed a fistula between the esophagus and trachea just above the bifurcation of the trachea.

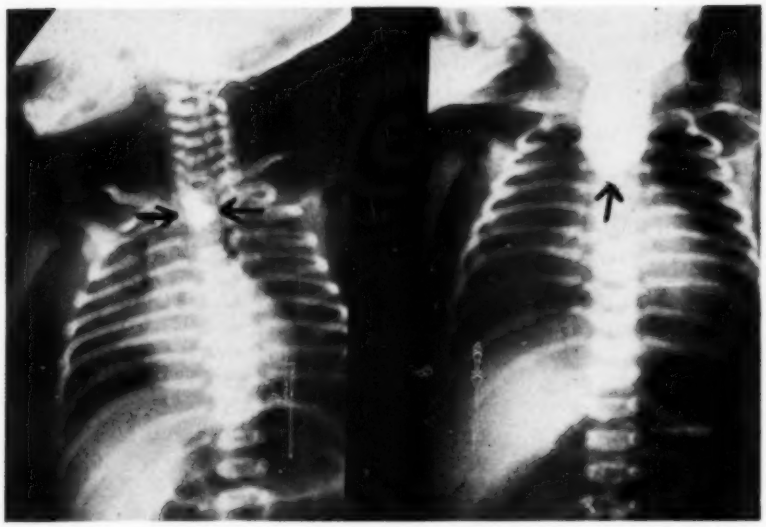

Fig. 4. Case 3: Upper segment of the atresic esophagus filled with lipiodol. (Contour of esophagus slightly retouched.)

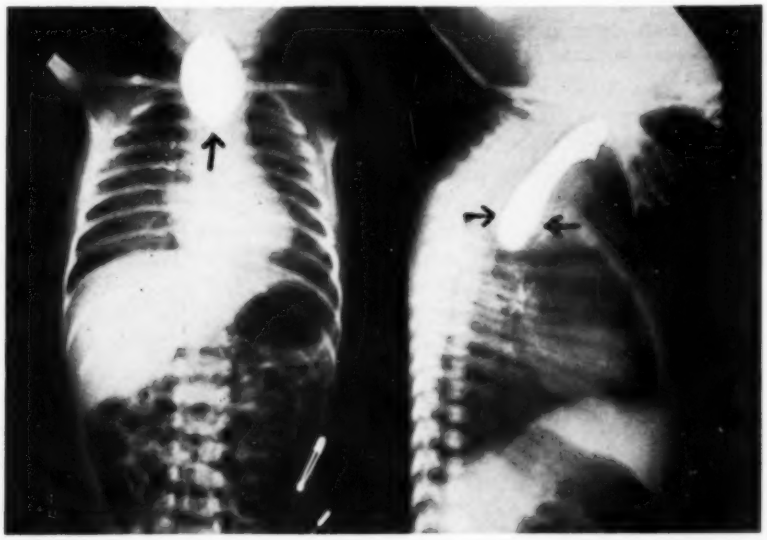

Fig. 5. Case 4: Moderately dilated upper segment of atresic esophagus demonstrated by lipiodol. Some lipiodol aspirated into right bronchus.

CASE 4: E. F. N., a three-day-old white boy, was admitted to the University Hospital with a history of regurgitating everything taken by mouth since birth. Delivery had been normal; the weight at birth was 6.5 pounds. The family history was unimportant. Physical examination and laboratory data revealed nothing unusual.

Roentgen studies showed an atresia of the esophagus at about the level of the fourth dorsal vertebra (Fig. 5). The stomach contained a moderate amount of gas, indicating a tracheo-esophageal fistula.

Gastrostomy was done and a No. 13 French catheter was passed into the stomach and threaded into the lower esophagus through its cardiac orifice. After passing the catheter upward about 5 cm., 2

c.c. of 5 per cent sodium hydroxide were injected into the esophagus to produce a lye burn stricture. The child died on the fifth postoperative day, and autopsy was not granted.

SUMMARY

Four cases of congenital atresia of the esophagus, all associated with tracheo-esophageal fistula, have been presented. The embryology, symptomatology, diagnostic, and therapeutic procedures have been discussed.

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Roentgenologic Manifestations and Clinical Symptoms of Rib Abnormalities[1]

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During a period extending from January 1930 to June 1942, the Department of Radiology at the University of Colorado Medical School and Hospitals made 38,105 roentgenograms of those portions of the body which lend themselves specifically to a study of rib abnormalities. This includes all roentgenograms of the spine, chest, and abdomen. Among the number there were found 59 rib abnormalities (0.15 per cent of the total).

For purposes of simplification, the anomalies have been grouped into seven classifications: (1) cervical ribs; (2) lumbar ribs; (3) bipartition, or "forking" of the anterior end of a rib; (4) synostosis, or bony union of adjoining ribs; (5) "tile-roof" ribs, or imbrication of ribs; (6) rudimentary ribs; (7) other deformities.

CERVICAL RIBS

Nineteen instances of cervical ribs, or 32 per cent of the 59 cases, were seen. Details as to their number, length, occurrence unilaterally or bilaterally, and whether they were jointed or non-jointed, are given in Table I. In every instance the cervical ribs were contingent to the seventh cervical vertebra. Two observations of interest were made: (1) the average length of the right cervical ribs (44.4 mm.) was slightly greater than the average length of the left cervical ribs (37.5 mm.); (2) the incidence of jointed ribs was only slightly greater than that of non-jointed ribs, the ratio being 17 to 14. The longest cervical ribs were of the jointed variety, the longest right rib measuring 85 mm. and the longest left rib 70 mm. The shortest cervical ribs were non-jointed and measured 22 mm. for both the right and left sides. Figure 1 shows an illustrative case.

TABLE I: CERVICAL RIBS

Side	Number	Longest (mm.)	Shortest (mm.)	Average Length (mm.)
Bilateral				
Right	12	85	22	42.5
Left	12	70	22	37.8
Unilateral				
Right	3	60	40	50.0
Left	4	35	25	30.0
Jointed				
Right	9	85	25	66.0
Left	8	70	28	46.0
Non-jointed				
Right	6	38	22	28.0
Left	8	38	22	29.0
Total				
Right	16	85	22	44.4
Left	15	70	22	37.5

Association with symptoms has been grouped as a very positive correlation; a slightly positive correlation; and a negative correlation. In 10, or 52.6 per cent, of the cervical rib cases there was a very positive correlation. In these cases the chief complaint was pain. In 6 this was localized to the back of the neck, and in the remaining 4 cases it radiated to the shoulder or supraclavicular region. There was no instance of neuromuscular disturbances of the hands or arms. In 3, or 15.9 per cent, of the cases, the patient had complained of vague pain localized to the shoulder joint, suggestive of a bursitis. These 3 cases were regarded as showing only an indication of correlation. In the remaining 6, or 31.5 per cent of the cases, symptoms were not at all referable to the cervical ribs and the correlation was classed as negative. In 68.5 per cent of the cases of cervical ribs, therefore, there was an association of symptoms with the presence of the anomaly.

While age was of no significance, it is of interest that the range of the group was

[1] From the Department of Radiology, University of Colorado School of Medicine and Hospitals, Denver, Colorado. Accepted for publication in September 1942.

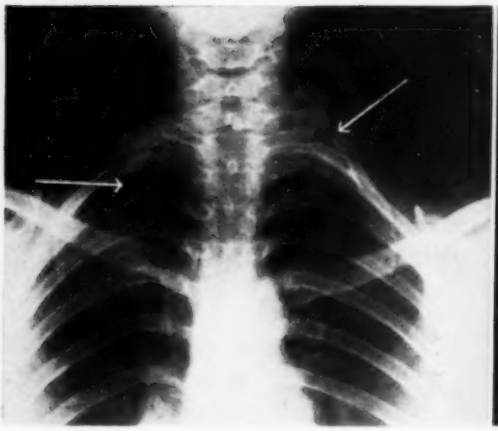

Fig. 1. Bilateral cervical ribs.

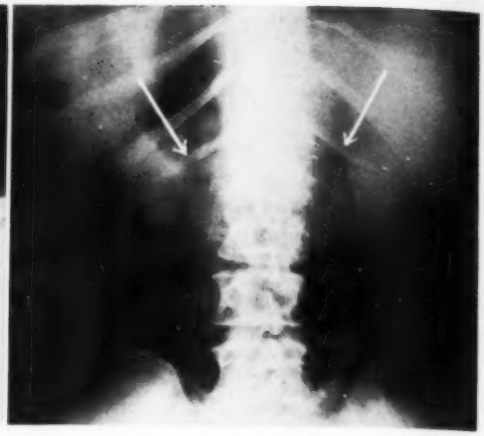

Fig. 2. Bilateral lumbar ribs.

from eighteen to fifty-six years. More than two-thirds of the patients were females (Table III), there being 13 females and 6 males. Because of the small size of the series, however, no conclusions can be drawn from these figures.

LUMBAR RIBS

Seventeen (29.3 per cent) cases of lumbar ribs were found. As shown in Table II,

TABLE II: LUMBAR RIBS

Side	Number	Longest (mm.)	Shortest (mm.)	Average Length (mm.)
Bilateral				
Right	16	68	10	39.0
Left	16	70	25	38.2
Unilateral				
Right	1	65	..	65.0

in all cases except one this anomaly was bilateral. In the one unilateral case the rib occurred on the right side and was extremely long, measuring 65 mm. In every instance the lumbar ribs were contingent to the first lumbar vertebra. The longest lumbar rib measured 70 mm. and occurred on the left side, while the shortest rib measured 10 mm. and occurred on the right side. Figure 2 is an example of this group.

Of the 17 cases of lumbar ribs, 12 (70.6 per cent) were associated with clinical symptoms. Eight patients complained of severe pain in the back, 3 of soreness or backache, and one of a catching pain in his back. In one case there was only an indication of correlation, a marked lordosis associated with some backache. In the remaining 4 cases (24.9 per cent) there was no correlation.

The age range was from fifteen to fifty-nine years. As in the case of the cervical ribs, there was a predominance of females, 12 females to 5 males (Table III).

TABLE III: SEX DISTRIBUTION

	Male	Female
Cervical ribs	6 (31.6%)	13 (68.4%)
Lumbar ribs	5 (29.3%)	12 (70.7%)
Bipartition	4 (80.0%)	1 (20.0%)
Synostosis	5 (100.0%)	.. ..
"Tile-roof"	3 (75.0%)	1 (25.0%)
Rudimentary ribs	4 (80.0%)	1 (20.0%)
Other deformed ribs	3 (75.0%)	1 (25.0%)
Total	30 (50.9%)	29 (49.1%)

BIPARTITION

In 5 cases bipartition or bifurcation of one or more ribs occurred. In 2 patients the first right rib and in 2 others the fourth right rib was affected. Figure 3 shows one of the latter cases. In the fifth patient the seventh, ninth, and tenth left ribs were bifurcated, the forks being from 20 to 50 mm. in length.

In one of these cases there was an apical

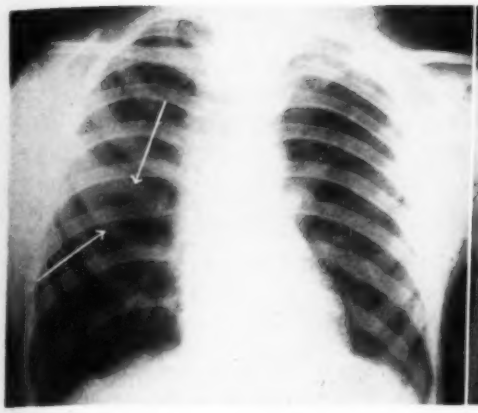

Fig. 3. Bipartition of ribs.

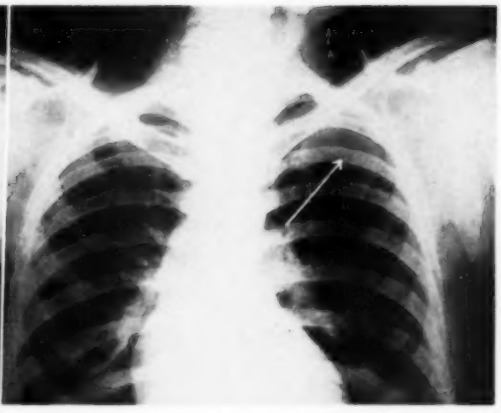

Fig. 4. Synostosis of ribs.

tuberculous lung lesion. Schedtler in his article on rib abnormalities (1) states that narrowing of the apical portion of the thorax due to an abnormality of a first rib predisposes to tuberculosis. In this instance the lesion was in the lung apex behind the affected rib. This was regarded as positive correlation between rib abnormality and clinical findings. In the remaining 4 cases there was no correlation with clinical symptoms or findings.

Schedtler (1) observed that bipartition usually involves the right fourth rib, though he offers no explanation of this. In 2 of the 5 cases in the present study the right fourth rib was affected.

The age group extended from five to fifty-three years. Oddly enough, 4 (or 80 per cent) of the patients were males (Table III), though the group is too small to permit conclusions.

SYNOSTOSIS

Synostosis, or bony union between adjoining ribs, was seen 5 times. In 3 instances the synostosis occurred between the first and second left ribs anteriorly. The appearance in these 3 cases was uniform, the synostosis giving the appearance of an extremely broad first rib. One of these cases is shown in Figure 4. In the remaining 2 cases the synostosis was very slight, occurring between the third and fourth right ribs in one patient, and the fourth and fifth right ribs in the other patient. Simon, in discussing rib abnormalities (2), speaks of synostosis occurring posteriorly in the region of the neck of the rib. No case in our series was of this variety.

Correlation with symptoms and clinical findings was positive in 2 patients, both of whom had tuberculous lung lesions in the apex directly behind the synostosis. In the remaining 3 cases no correlation was evident. The age limits in this group were nine and forty-four years. All 5 patients were males (Table III).

"TILE-ROOF" RIBS

"Tile-roof" formation, or imbrication of ribs, is a rare condition. In this study there were only 4 cases, or approximately 0.01 per cent of the entire group studied. Figure 5 is illustrative of this condition. In 3 of the 4 patients the anomaly was bilateral, giving a symmetrical appearance, while in the fourth the condition, while bilateral, was more marked on the left.

In 3 of the group lung pathology, pneumonia or tuberculosis, was the chief clinical factor. The fourth patient had symptoms referable to the chest (chronic cough, etc.), though no definite pulmonary lesion was present. The clinical symptoms and findings were compatible with this anomaly, in which the thoracic cage is partially collapsed.

The age limits of this group were fifty-

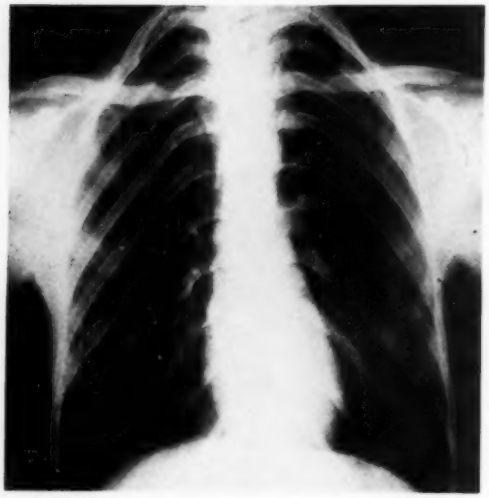

Fig. 5. Imbrication (tile-roof formation) of ribs.

one and seventy-eight years. Three of the patients were males (Table III).

RUDIMENTARY RIBS

Only 5 examples of rudimentary ribs were found. A case was placed in this group if one or more ribs were definitely undersized as compared to the neighboring ribs. In every instance the first rib alone was involved. The condition was bilateral in 3 cases, while in the remaining 2 the affected rib was on the left. In each case the underdevelopment amounted to 20 to 30 mm.

There was no correlation with clinical symptoms in any of the rudimentary rib cases. The age limits were twenty-eight and fifty-nine years. There were 4 males and 1 female in this group (Table III).

OTHERWISE DEFORMED RIBS

Four examples of congenitally deformed ribs not falling into any preceding classifications were found and each case differed from the others. In two patients the right ribs (3rd, 4th, and 5th in one; 5th in the other) deviated internally. In one case the 8th left rib was widened, and in the remaining case the 7th right rib was deformed posteriorly.

As in the preceding group, there was no correlation with clinical symptoms. The age limits were thirty and fifty-one years. There were 3 males and 1 female (Table III).

SUMMARY

Rib abnormalities were discovered in 59 of a series of 38,105 roentgenograms, approximately 0.15 per cent. Cervical and lumbar ribs accounted for 36 cases, or over half the total. The remaining anomalies consisted of bipartition, synostosis, "tile-roof" formation, rudimentary ribs, and otherwise unclassified deformities.

In 22 cases pain was the chief complaint and its localization very definitely associated it with the presence of a rib abnormality. In 7 cases the lung parenchyma was affected, 6 patients having tuberculosis and 1 pneumonia. In each of the latter 7 cases the pathological condition was correlated with an affected first rib or a partially collapsed thoracic cage due to "tile-roof" formation of the ribs. In 33 of the cases there was an indication of correlation of symptoms with rib abnormalities, while in the remaining 26 cases there was no correlation. In 17 of these 26 cases the rib abnormality was of such a nature that no physiological or anatomical disturbance was to be expected.

Age played no significant role, the patients ranging from five to seventy-eight years. In the series as a whole, sex also appeared to be of little significance, 30 patients being males and 29 females.

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Experimental Modification of Radiosensitivity of Embryonic Cells[1]

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EXPERIMENTS IN which the radiosensitivity of cells has been studied indicate that different cells and tissues respond to x-irradiation in various ways. Other experiments in which the radiosensitivity of cells has been altered experimentally by changing their physiological activity show that the same modifying agent does not always change the sensitivity of different types of cells and tissues in the same way. Thus, some investigators (Holthusen, 17; Dognon, 8; Politzer, 27; Packard, 25) have found that low temperature during irradiation increases resistance, while others (Mottram, 24; Crabtree and Cramer, 7; Petry, 26; Ancel, 1; Ancel and Vintemberger, 2; Henshaw and Francis, 15), using other types of cells, have shown that low temperature either increased or had no effect on radiosensitivity.

Lambert and Firket (18–21) studied oxygen consumption, water uptake, and mitotic activity of pea seedlings at different stages of development but were unable to correlate radiosensitivity with any of these factors. Henshaw and Francis (15, 16) obtained similar results with wheat seedlings, and in further experiments found that, when the development of germinating seedlings was inhibited by dehydration or by anaerobiosis, the radiosensitivity, as measured by subsequent growth rate, was decreased. Thus it seems obvious that, while radiosensitivity may be modified experimentally, the results obtained with different cells and organisms vary even when the same experimental method is used.

The present experiments were undertaken in an attempt to obtain information concerning the effect of low temperature and dehydration on the radiosensitivity of embryonic cells of the grasshopper and to determine whether or not these effects were constant at different stages in the development of the organism.

MATERIAL AND METHODS

The egg of the grasshopper, *Melanoplus differentialis*, was chosen as the experimental material, since the changes in its radiosensitivity at different developmental stages have been studied by Evans (9–12) and because various aspects of its physiological activity have been examined by Bodine and others (3, 4, 5, 14, 30, 35, 36).

Eggs of this species, when kept at a constant temperature of 25° C., develop for approximately twenty-one days (prediapause period), at the end of which time they enter a period of developmental block (diapause). If they are then placed at a low temperature (below 10° C.) for two to three months, upon return to constant high temperature (25° C.) they will undergo further development (post-diapause) and hatch on about the eighteenth day. The morphological changes taking place during development have been carefully recorded by Slifer (31), and the developmental stages studied in the present experiments are expressed as days at 25° C., since Slifer has described the embryos in these terms.

The effects of low temperature and dehydration on the morphological development and oxygen consumption of this material are rather well known. It has been shown by Bodine (3, 4) that if developing eggs are subjected to a low temperature (5–10° C.) their morphological development will be stopped as

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TABLE I: LOSS IN WATER CONTENT OF GRASSHOPPER EGGS DURING DEHYDRATION

Age (days)	Loss in Weight (per cent)	Loss in Water Content* (per cent)	Length of Drying Period (hours)
Pre-diapause			
1	4.10	9.10	6.0
1	7.63	16.94	13.0
3	4.83	10.72	13.0
5	4.86	10.79	13.5
8	6.21	13.79	13.0
15	7.81	17.34	18.0
Post-diapause			
2	4.05	6.95	14.0
2	4.93	7.25	16.0

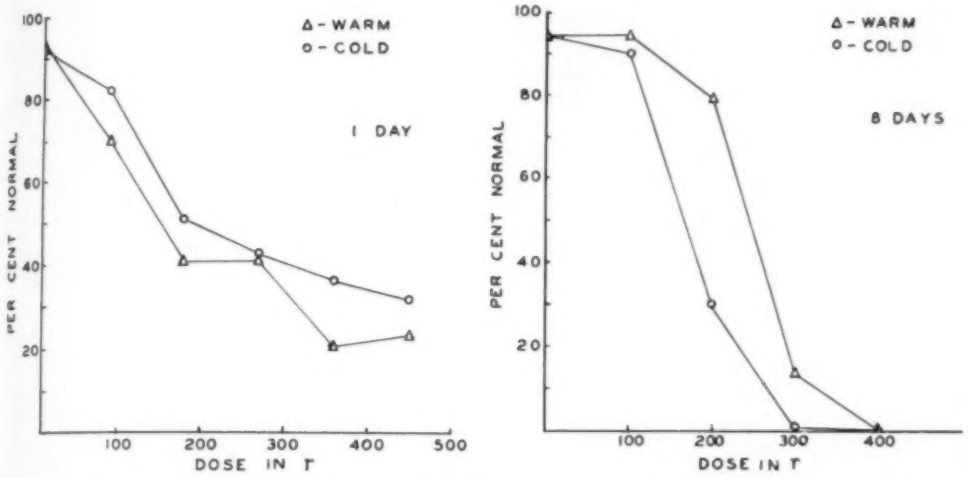
* Calculated using Dr. E. Slifer's (unpublished) data for the total water content of eggs of various ages.

long as they are kept at that temperature. Goodrich and Bodine (14) have found that developing eggs consume oxygen at a very much slower rate at 15° C. than they do at 25° C., and it is safe to assume that at still lower temperatures the rate of oxygen consumption would be further reduced.

According to the data of Thompson and Bodine (35), post-diapause eggs which were dehydrated to the same extent as the dehydrated eggs used in these experiments show a small decrease in oxygen consumption. Similarly, the data of Schipper (30) indicate that oxygen consumption of pre-diapause eggs is slightly decreased and development is somewhat impeded by short periods of dehydration. In the present experiments, examination of eggs which had been dehydrated for from thirteen to eighteen hours showed that they had attained nearly the same stage of morphological development as had moist eggs of the same chronological age. Thus it seems apparent that temperatures below 10° C. stop development and markedly reduce oxygen consumption, and that short periods of dehydration impede both development and oxygen consumption to a smaller extent.

Eggs of the desired age were washed free of débris and divided into two lots. In each experiment one lot was irradiated at a low temperature (1°–3° C.) and the other at a high temperature (25° C.). The temperature of the eggs during irradiation was maintained at a constant level by placing them in a shallow plastic dish held, by an aluminum support, at the surface of water at a desired temperature in a thermos jug. The mouth of the thermos jug was covered by cardboard, 1 mm. in thickness, which provided adequate heat insulation and had only a slight filtering action on the radiation. Eggs treated in this manner attained the temperature of the water in the thermos jug within about fifteen minutes and were maintained at this temperature for at least thirty minutes before irradiation was started. The temperature of the eggs was measured several times during each experiment by means of a thermocouple placed beside them and was always found to be constant within 1° C. during the course of the irradiation. Unirradiated eggs which were used as controls for each irradiated lot were kept at the same temperature as the irradiated eggs. A series of doses of x-rays was given by removing samples of eggs from the plastic dish at appropriate intervals during the irradiation. After irradiation the eggs were placed on moist filter paper in caster dishes and put in a constant temperature chamber maintained at 25° C.

In the experiments in which the effect of dehydration on radiosensitivity was to be studied, washed eggs of the desired age were divided into two groups. Group A was placed in a $CaCl_2$ desiccator at room temperature (about 23° C.) and allowed to dry for approximately thirteen hours. Group B was placed on moist filter paper and kept at 25° C. for the same period of time. About 200 eggs (to be used as controls) were removed from Group A and accurately weighed before and after desiccation to determine the amount of water lost during the thirteen-hour period of drying. As shown in Table I, eggs dried for this length of time lost from about 11 to 14 per cent of their original water content. Both moist and dehydrated eggs were irradiated at 25° C. in the manner already described and were placed on moist filter paper immediately following irradiation. They were then put



Figs. 1 and 2. Dose-survival curves for eggs irradiated warm and cold on the first day and on the eighth day.

at a temperature of 25° C. and kept at that temperature until they were examined.

In all the experiments on pre-diapause eggs the eggs were allowed to develop until well into diapause. At this time the embryos were dissected out and examined under a wide-field dissecting microscope. Post-diapause eggs were put on moist sand in cotton-stoppered shell vials after irradiation and allowed to hatch there.

For the irradiation a mechanically rectified x-ray machine was used which was operated at 130 kv.p. and 5 ma. The radiation was unfiltered except for 2 mm. of cardboard which was used to avoid heating effects. The target distance was 26 cm. and the intensity under these conditions was 182 r/minute, as measured in air by a Victoreen dosimeter.

EXPERIMENTAL RESULTS

Effect of Low Temperature (1°–3° C.) on Sensitivity: The effect of irradiating eggs while they were at 1° C. was studied on the subsequent development of eggs rayed on the first, second, third, fourth, fifth, eighth, fifteenth, and nineteenth day pre-diapause and on the hatching of eggs irradiated at twelve hours and two days post-diapause. Representative data are shown graphically in Figures 1 to 3. In all dose-survival curves each point represents data from 200 to 500 eggs; about 40,000 eggs were examined in all. For the purposes of these experiments an embryo was considered to be normal if no gross morphological injury could be detected under the dissecting microscope.

Eggs irradiated at 1°–3° C. on the first or second day of pre-diapause development show a greater radioresistance than those rayed at 25° C. (Fig. 1), but on the third day there is no apparent effect of the low temperature on subsequent development. On the fourth day, however, and in all other pre-diapause developmental stages studied, eggs irradiated at 1°–3° C. are more susceptible to radiation injury than are those irradiated at 25° C., the greatest difference being apparent in eggs rayed on the eighth day (Fig. 2). The sensitivity of post-diapause eggs (Fig. 3), as measured by the per cent hatched, is strikingly increased when they are irradiated at 1°–3° C.

The form of the curves for one-day to eight-day pre-diapause eggs irradiated at 25° C. and the dosages required for injury are quite comparable to the results obtained by Evans (11), who studied the effects of x-rays on the subsequent development of one-day to twelve-day pre-diapause eggs. It has been shown by Evans (12) and Carothers (6) that when

eggs are irradiated early in development (one to two days), the yolk and serosa cells are less affected by irradiation than are cells of the embryo. It seemed desirable, therefore, to study on these cells the effect of low temperature during irradiation. Slifer (32) has found that the chitinous cuticle surrounding the grasshopper egg is secreted by the serosa cells during the sixth to the fourteenth day. The presence or absence of a cuticle, therefore, may be considered an index of the x-ray injury to serosa cells. Two-day predia pause eggs were given a series of doses of radiation at 25° C. in the manner previously described, and the eggs were examined on the fourteenth day for the presence of a cuticle. Serosa cells are found to be no more sensitive when irradiated at 1°–3° C. than when irradiated at 25° C.

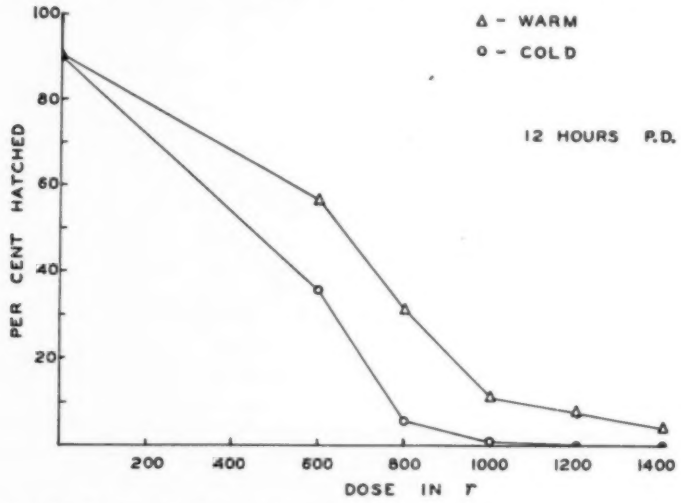


Fig. 3. Dose-survival curve for eggs irradiated warm and cold at twelve hours post-diapause.

Effect of Dehydration on Sensitivity: The effect of irradiating eggs while they were dehydrated was studied on the subsequent development of eggs rayed on the first, third, fifth, eighth, and fifteenth day pre-diapause and on the hatching of eggs rayed on the second day post-diapause. Typical curves are shown in Figures 4 and 5. Each point on the curves represents data for from 200 to 500 eggs. A total of about 20,000 eggs was examined in these experiments. Three-day eggs are slightly more sensitive to radiation when rayed while dehydrated, but the sensitivity of five-day eggs is apparently not changed when they are dry during irradiation. Eight-day and fifteen-day (Fig. 4) predia pause eggs and two-day post-diapause eggs (Fig. 5) are less sensitive when x-rayed while dry.

According to a theory which Failla (13) has proposed as to the mode of action of x-rays on mammalian tissue, the effect of the radiation is to produce "radio-ions" in the cells and the fluid bathing them. In mammalian tissue, the fluid bathing the cells is constantly flowing past them and hence carries away the "radio-ions" newly formed in the fluid by the ionizing radiation. Since the cell membrane may be impermeable to some or all of the "radio-ions," the result is an increase in the osmotic pressure of the cell leading to the characteristic cell swelling which occurs in many irradiated mammalian tissues. This theory has been used by Failla to describe the method of x-ray injury only for mammalian cells which exhibit a characteristic swelling reaction following ir-

radiation. Consequently the theory is not strictly applicable to the grasshopper egg, since it is a closed system, except for a slow passage of water into the egg, and to mammalian tissue would obtain and Failla's theory could be tested on this invertebrate material. This may be done by removing the chorion from the egg, thus

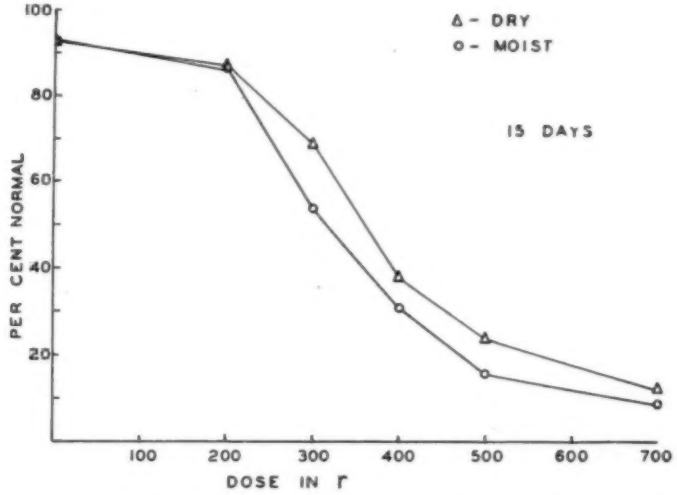


Fig. 4. Dose-survival curve for eggs irradiated dry and moist on the fifteenth day.

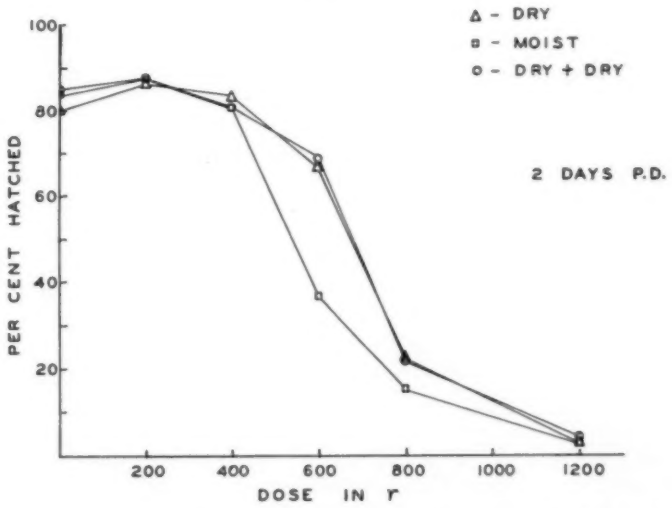


Fig. 5. Dose-survival curve for eggs irradiated on the second day post-diapause. Effect of drying during irradiation (triangles) and both during and for twelve hours after irradiation (circles).

since there is no evidence that the cells of the grasshopper embryo swell following irradiation (see Carothers, 6). If, however, the slow water exchange could be speeded up, then a condition somewhat analogous permitting a very much more rapid passage of water into and out of the egg. In some preliminary experiments on dechorionated two-day post-diapause eggs it has been possible to show that dehydrated

eggs which were kept dry for twelve hours after irradiation were considerably more resistant (as measured by subsequent hatching) than dehydrated eggs which were moistened immediately after irradiation. This is the result which the theory would predict, since keeping the eggs dry for a period after irradiation would allow time for the recombination of the "radio-ions" to occur inside the cell, thus reducing the increased intracellular osmotic pressure before a large flow of water past the cell resulted in osmotic swelling. If, however, the chorion is left on the egg and water exchange is slow, then the extra period of drying after irradiation should have little or no further effect on radiosensitivity. These are the results which have been obtained (Fig. 5).

The median-effect-dose (M.E.D.), or that dose which results in the injury of 50 per cent of the embryos, has been calculated from each curve. The ratio of the median-effect-dose for eggs of a given age rayed at 1°–3° C. to that for eggs rayed at 25° C. is an index of the difference in the effect of the low and high temperatures during irradiation. Similarly, the ratio of the median-effect-dose for dehydrated eggs to that for moist eggs has been calculated. These data for the effect of low temperature or dehydration on eggs at all the stages of development examined are summarized in Figure 6. It is obvious that the effect of irradiation at 1°–3° C. is not constant during the course of development, but changes from increased protection for one-day and two-day eggs to decreased protection during all the rest of the pre-diapause period and for the part of the post-diapause period studied. The effect of dehydration, also, is not constant, the change occurring at about the same time but in the opposite direction. The data for eggs dehydrated for either six or thirteen hours on the first day show that they are apparently not different in their reaction from eggs of the same age rayed in the moist condition. These curves, however, are based on a relatively small number of eggs (50 to 100 eggs per dose).

DISCUSSION

Attempts to correlate changes in the effects of low temperature and dehydration on radiosensitivity with cytological changes in the developing grasshopper egg have not been highly successful. Cytological events occurring during the early development (at 25° C.) of the grasshopper egg have been studied by Slifer and King (34). The effect of the low temperature is to decrease the sensitivity during the time when undifferentiated segmentation nuclei are present (first and second days) and to increase the sensitivity at about the time of the formation of the germ band (third or fourth day). The change in sensitivity with dehydration appears to take place not more than two days later (Fig. 6), coincident with the appearance of a definitely formed embryo in which the germinal layers are present.

The physiological changes in the developing egg are very little more helpful in obtaining an explanation for the observed results. Slifer (33) has shown that the water content of pre-diapause eggs does not change during the first week of development and that it increases slowly after the seventh day. Since, during the first eight days, marked changes occur both in the normal sensitivity (Evans, 10, 11) and in the effect of dehydration and low temperature on sensitivity, it seems unlikely that the normal, slow change in water content could offer any explanation for the sensitivity changes.

Oxygen consumption of the grasshopper egg has been measured by Bodine (4) and by Boell (5), who have shown that the oxygen uptake increases steadily until about the twentieth day pre-diapause, when it abruptly declines with the onset of diapause. It would seem that here again one can find no explanation for the changing effect of low temperature and dehydration.

Boell (5) has also measured the respiratory quotient (R.Q.) of the grasshopper egg in all stages of development. He finds that the R.Q. steadily declines from a high value of 0.95 on the first day

to a low value of about 0.60 from the sixth to the ninth day. It then rises to a value of about 0.70 on the fifteenth day and is maintained at that level throughout the remainder of pre-diapause, all of diapause, and the first two days of post-diapause. These changes in the R.Q. during pre-diapause parallel very closely the changes in radiosensitivity with low temperature during that period (Fig. 6). Boell has interpreted the R.Q. curve to mean that following a short period of carbohydrate oxidation (on the first day) the R.Q. is modified by special synthetic processes until about the fifteenth day, when it (0.70) indicates that fat is being oxidized predominantly. This point of view is strengthened by the work of Thompson and Bodine (36), who found that the decline in the amount of pyrophosphate in the grasshopper egg was approximately coincident with the change in the R.Q. Lohmann (22) has considered that pyrophosphate indicates the amount of adenyl-

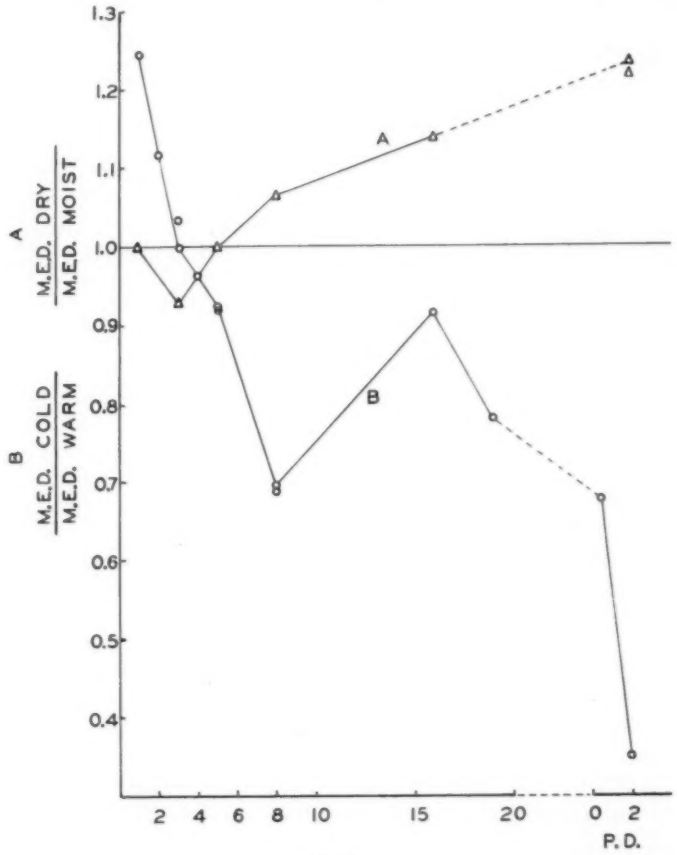


Fig. 6. Summary of results. Ordinate: Ratio of M.E.D. dry to M.E.D. moist (triangles, curve A), and ratio of M.E.D. cold to M.E.D. warm (circles, curve B). Abscissa: Days of development. Broken line on abscissa indicates diapause period. All values above the line drawn through 1.0 on the ordinate indicate increased resistance cold or dry. Values below the line indicate decreased resistance cold or dry. Two points on curve A for 2 days post-diapause, and on curve B for 3, 5, and 8 days pre-diapause are values for duplicate experiments.

pyrophosphate, a co-enzyme concerned in carbohydrate metabolism. The parallelism between the change in R.Q. and the change in effect of low temperature on sensitivity suggests that these factors may be closely related. It may be that when carbohydrate is being oxidized (on the first day) the effect of the low temperature during irradiation is to inhibit the functioning of some mechanism associated with carbohydrate oxidation which tends to intensify the effects of radiation on the cells, and that as fat-oxidizing mechanisms begin to function, the effect of low temperature is to inhibit the functioning of some mechanism associated with fat oxidation which tends to protect the cells from the effects of radiation. It may well be, however, that the parallelism between the R.Q. curve and the curve expressing the change in effect of low temperature on sensitivity is entirely fortuitous, and a relationship such as that suggested above must be considered as speculative until further evidence is at hand.

So far as is known, the only common effects of low temperature and dehydration on the grasshopper egg are inhibition of development and reduction in rate of oxygen consumption. As pointed out in an earlier section, low temperature effects a complete stoppage of development and a marked decrease in rate of oxygen uptake, while dehydration, at least to the extent used in these experiments, results in a smaller decrease in both developmental rate and oxygen uptake. From the results obtained it is obvious that the effects noted are not due simply to inhibition of development but arise as a result of a more specific action of low temperature or dehydration on the cells. From the different effects of these two agents it seems apparent that they do not act in the same way. As suggested above, it is quite possible that low temperature modifies the oxidative mechanisms or some process or processes associated with them, while the effects of dehydration may be due to changes in the osmotic relations of the cells to the fluids bathing them.

An interesting suggestion regarding the possible effect of low temperature in modifying radiosensitivity is provided by genetic studies. Mickey (23) has shown that when *Drosophila* males were rayed at a low temperature (4° C.) a significantly greater number of translocations were observed than when the flies were irradiated at a high temperature (28 to 33° C.). Similarly, Sax and Enzmann (29) and Sax (28) found a larger number of chromosome breaks when *Tradescantia* microspores were irradiated at a low temperature (3° C.). The explanation suggested by Sax (28) for these results is that at high temperatures fusion of broken chromosomes is accelerated and many of the broken ends are reunited in the original position, while at low temperatures fusion is delayed and broken ends may fuse in abnormal ways to produce chromosome aberrations. If this explanation for the effect of low temperature is to be applied to the cells of the grasshopper egg, it is necessary to assume that the physical state of the chromosomes which permits such fusions is different in young (one and two days) and in older eggs. A further test of this explanation as it may be applied to the grasshopper egg awaits additional information concerning chromosome structure of these cells at various stages in development.

The particular value of the present experiments is to show that radiosensitivity of the cells may be modified in opposite directions by the same modifying agent at different stages in their development. This unique situation presents a basis for further experiments which should result in a more intimate understanding of the processes involved in cell radiosensitivity.

SUMMARY

1. The sensitivity of cells of the grasshopper egg to x-rays at various developmental stages has been modified by low temperature and by dehydration during irradiation.

2. The effect of low temperature is to decrease sensitivity before the third day

of pre-diapause development and to increase sensitivity during the remainder of pre-diapause and the first two days of post-diapause.

3. Dehydration causes an increase in sensitivity before the fifth day of pre-diapause development and a decrease in sensitivity during the remainder of pre-diapause and on the second day post-diapause.

4. Possible mechanisms through which these effects may be produced are discussed.

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Clinico-Pathological Conference[1]

HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PENNA.

Philip J. Hodes, M.D., J. S. Forrester, M.D., J. S. Lockwood, M.D.

S. S. (Case H0251), a 43-year-old Jewish woman, was first admitted to the University Hospital in August 1941, complaining of pain in the right cheek and swelling of the right submaxillary and cervical lymph nodes of eight months' duration. During this illness anorexia and vomiting developed and the patient had lost 30 pounds of weight. For three months there had been a painless lump in the right breast, and for several weeks before admission she had experienced pain in the left shoulder and upper abdomen.

The initial physical examination showed a pale, chronically ill female with mild exophthalmos. Careful oral study revealed the presence of soft masses in the right cheek and a possible bulging of the right alveolar ridge. The right breast contained a hard, irregular mass, measuring 5 × 7 cm., not definitely attached to skin or muscle, but adherent to the areola (Fig. 1A). There was a mass in the right axilla the size of a walnut. The left breast contained a smaller mass in the upper outer quadrant (Fig. 1B). There was one enlarged node in the right inguinal region. The liver and spleen were both slightly enlarged. Large masses were present in the lower abdomen, thought to be attached to the uterus.

Results of all laboratory studies, including the blood count, were normal.

Roentgenograms of the sinuses showed chronic disease of both antra with polypoid changes on the right side. Roentgenograms of the mandible and chest were noncontributory.

A biopsy of the mass in the right breast and the right inguinal node was obtained.

The patient was discharged to the outpatient department after four weeks, having shown slight improvement during hospitalization.

In November 1941, three months after her first admission, the patient was readmitted to the hospital with the added complaints of rapid increase in the size of the abdomen, dyspnea, and cough. Her menstrual periods, which had been scanty for a year, had ceased altogether for the past two months.

At this time, physical examination showed emaciation, two masses in the right breast and five smaller ones in the left, and an abdominal mass which had increased greatly in size since the previous admission. Pelvic examination showed an enlarged irregular uterus and at least one large mass distinct from the uterus, which was thought to be an ovarian tumor.

Because of extreme discomfort, operation was advised and a bilateral salpingo-oophorectomy was performed in December 1941. This was followed by recurring ascites and diminishing serum protein. The patient failed rapidly and died in January 1942, twelve months after her first symptoms and five months after her first hospitalization.

Dr. Lockwood: This is a very unusual case. The patient presented evidence of a chronic wasting disease with a mass in each breast, enlarged nodes in the right axilla, and an abdominal mass or masses, which increased rapidly in size a month before death. Superficially, this looks like carcinoma of the breast with widespread metastases with possibly a coincidental uterine or adnexal tumor. Before continuing the discussion, however, I would like to read into the record the note made by Doctor Eliason at his first examination before the biopsy. "This woman has a large, plate-like mass in her right breast which feels like the masses one feels in chronic cystic mastitis with large areas of

[1] This report was prepared by Robert Phelps Barden, M.D.

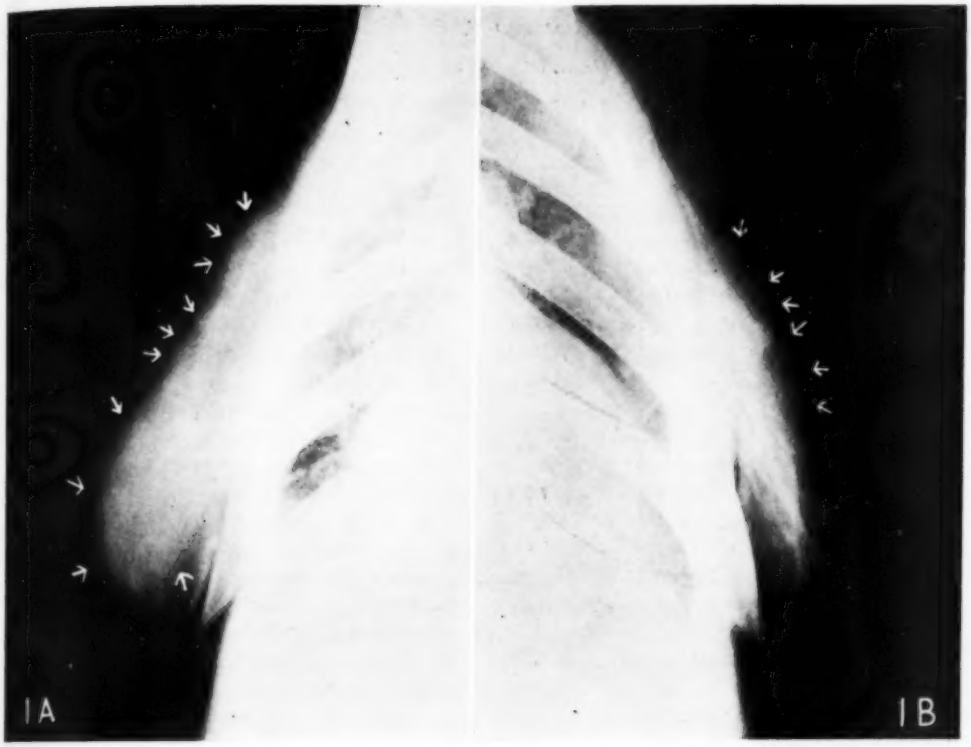

Fig. 1A. Roentgenogram of the right breast made with the patient standing in the right anterior oblique position. Note the dense mass which is infiltrating practically the entire breast and pectoral muscles.
Fig. 1B. Roentgenogram of the left breast made with the patient standing in the left anterior oblique position. Note the two circumscribed masses in the upper portion which are apparently encapsulated.

cystic degeneration. The multiple nodules in the left breast might also fit this picture. I cannot quite decide about the mass in the right axilla. I do not think it feels like a metastatic node from primary carcinoma of the breast. It may be an expression of widespread lymph node disease. From this examination, my only suggestion would be that the patient has bilateral cystic mastitis with the possibility of some superimposed neoplasm on the right side."

There are several important findings that should not be overlooked: first, the report of the dental surgeon of the masses in the right cheek; second, the history of nodes being enlarged in the right side of the neck, with the finding on admission of a solitary node in the right groin and a palpable spleen. The third and most important single point is the question as to the relation of the lumps in the breast to the abdominal mass. In view of its rapid increase in size, and the ascites, I take it this abdominal mass was not a fibroid, as reported in the first gynecologic consultation.

Because of the diffuse nature of the disease, its spotty manifestation in widely separated lymph nodes, and the peculiar soft-tissue masses in cheek and breasts, I believe we are dealing with some type of lymphoblastoma, Hodgkin's, sarcoma, or leukemia.

Dr. Forrester: This patient received roentgen therapy over a period of several months. Will Doctor Hodes please discuss that aspect?

Dr. Hodes: Roentgen therapy was given intermittently from Oct. 2 to Dec.

27. We were influenced by the biopsy report, and treatment consisted of small doses of radiation to the right cheek and each breast and axilla. At first, intermediate voltage was used, but after it became apparent that the tumors were not particularly radiosensitive, high voltage and larger doses were employed. The total amount to each area was small, however, the maximum being 650 r total to the right cheek. Looking back now on the patient's course, I think we wasted valuable time, because we were afraid that this was a radiosensitive tumor and that large doses would kill the patient. As a matter of fact, more vigorous treatment might have materially prolonged her life.

Dr. Forrester: Are there any questions, before we discuss the pathology?

Dr. Miller: Why was the gynecological operation postponed so long?

Dr. Lockwood: Inasmuch as the biopsy indicated widely disseminated disease, it was deemed inadvisable to remove the abdominal mass while it was relatively asymptomatic. When it did begin to enlarge and ascites developed, it was too late.

Dr. Forrester: The sections from the first biopsy of the inguinal node were not easy to interpret. The predominant cell was an irregular vesicular one and mitotic figures were frequent. Eosinophiles were present in moderate numbers, with a fair amount of granulomatous elements. The capsule of the node was not invaded, and the picture was definitely not carcinoma. The most likely possibilities were leukemia and Hodgkin's disease.

The sternal puncture done a few days later showed nothing abnormal.

Subsequent sections were obtained by biopsy of the right breast and right axillary mass and these showed similar changes, which Doctor Fox and Doctor Bothe agreed were a cellular type of Hodgkin's disease. I might say here that it was the cellular character of the tumor and the numerous mitotic figures which suggested that it would be quite radiosensitive.

One month before death a bilateral oophorectomy was performed because of very large ovarian tumors. The sections were reported by Doctor Dunne, who felt that they were similar to the ones I have shown you today. He thought the growth was a malignant lymphoma of some type, although this type of tumor is very unusual in the ovary.

At autopsy practically every organ in the body was found to be invaded by tumor and all the lymph nodes were greatly enlarged. The histologic characteristics of many sections suggested lymphosarcoma rather than the ordinary type of Hodgkin's disease.

Clinical Diagnosis: Carcinoma of the breast. Uterine fibroid.

Doctor Lockwood's Diagnosis: Lymphoblastoma.

Diagnosis from Biopsy: Probable Hodgkin's disease.

Final Pathological Diagnosis: Lymphosarcoma.

Employer Is Liable in Common Law for Physician's Fees for Services Rendered Injured Employee[1]

I. S. TROSTLER, M.D., F.A.C.R., F.A.C.P.
Chicago, Ill.

THE QUESTION whether industrial commissions may legally fix the amount of medical fees for services rendered an injured person whose claims come before them for arbitration or adjustment is of considerable interest.

Industrial commissions in several states have at various times taken it upon themselves to determine or fix the amount of medical and surgical fees for injured employees whose cases had come before them for adjustment. In every instance, however, where the physician or surgeon has appealed from the decision of the commission, the courts have decided in his favor. Occasionally the decisions of the lower or trial courts have been against the physician, but in every such instance, the appellate and supreme courts have reversed these decisions and have held for him.

There is no question that under certain conditions, industrial commissions may fix the amount that *employers shall pay to an injured employee* for medical, surgical, or hospital services, when or if the employer fails to provide such services and the employee secures his own physician or surgeon; but in no instance and under no circumstances does the physician surrender his right to collect what he deems just and adequate payment for his services. Our contention has been, and the supreme courts of several states seem to hold with us, that physicians are not bound by and have nothing to do with the operation of the workmen's compensation laws. Their province is to attend the injured and their only connection with such laws lies in the fact that employers are required to furnish medical services to injured employees or pay for same if they (the employers) for any reason fail to furnish them. The fact that some employers either neglect or prefer not to furnish these services to their injured employees, but leave or permit the employees to select their own physicians, does not, cannot, and of right should not give anyone the right or the authority to fix the amount to be paid for the medical or surgical services rendered any more than it should empower or authorize the same body, group, or individual to determine what radio station the doctor may tune in on or the color of the neckties he should wear.

It is true, as has been stated, that the workmen's compensation laws in some states provide that the industrial commissions may fix the amount of medical and surgical fees that the employers shall pay to their employees. These laws make the employers and their employees parties to a contract, but *the physician is not a party to such contract unless he specifically agrees to enter into that contract.* These laws are for the protection of the employee who may be injured while at work and are *not for the physician* in any way or manner.

In the language of a learned judge:[2] "The meaning and intent of the workmen's compensation laws in every state are mainly and primarily intended for the protection of injured employees and the provisions regarding their receiving medical attention do not, cannot and are not intended to include the medical profession as such, in any sense."

The Illinois Appellate and Supreme Courts have decided, in several instances where cases were appealed from lower courts, that the industrial commission has no authority or right, as between the physician and his patient, to determine the amount of the fee to be charged or col-

[1] Accepted for publication in December 1942.

[2] Noer vs. G. W. Jones Lumber Co. (Wis.) 175 N.W.R. 784.

lected for any medical service. Similar decisions have been rendered by courts of last resort in Indiana, Georgia, Maine, Minnesota, New Jersey, New York, Oklahoma, Wisconsin, and other states.

In a recent decision from the Supreme Court of Indiana,[3] the following appears: "The appellant contends that the Workmen's Compensation Act, fairly interpreted, does not prevent his maintaining an action at law for medical services rendered by him under a contract with the employer; and that as to medical services rendered after the period during which the employer is compelled to furnish medical services, the Industrial Board does not have the 'power or authority to require such physician to submit such claims to the Industrial Board.' "

Farther along in this rather voluminous decision we read: "We can see no valid reason for saying that if the physician may maintain an action for such services in a court an employer would thereby be discouraged from assuming the obligation of employing a physician beyond the period required by the statute. . . . It was just as logical to assume that the legislature intended by paragraph 65 of the 1915 Act (and included in later acts I.S.T.) to make the fees of attorneys hired by the employer to represent it before the Industrial Board subject to the approval of the Industrial Board as to make the fees of physicians hired by the employer subject to the approval of the Industrial Board."

Concluding the Indiana decision, the Supreme Court said: "We hold that the Indiana Workmen's Compensation Act of 1929 did not deprive a physician of the right to recover in an action at law against an employer for services rendered to an employee, under a contract with the employer."

From the foregoing decision, and from decisions from nine other states, the writer believes that we can prove:

1. That, if employers authorize or give consent for physicians to attend injured employees, they, the employers, are liable for the physicians' fees.
2. That, if employers do not authorize or give consent for physicians to attend injured employees, the physicians' fees for services to these employees may be allowed by the industrial commissions; but that physicians who render their services to the injured employees are not in any way bound or obligated to accept the allowance or the amount of same made by the industrial commission unless they so desire, and that, not desiring to accept such fee, they may hold the employer or employee for the rightful amount of their fee and have the right to maintain action at common law.
3. That the fixing by industrial commissions of the amount to be paid by the employer to the employee for medical services does not and cannot fix the amount of the physician's fees and that this, as well as the foregoing statements, is upheld by all interpretations or constructions of the laws in every state in which this question has been decided by courts of last resort.

In conclusion, we are prepared to prove that the courts of last jurisdiction in ten states (and these are certain to be followed by others) have decided that we as physicians are not bound by the workmen's compensation laws as regards our fees and that nothing in these laws abrogates or abridges our right to recover for the amount of our fees by common law action.

A fund of information and references on this important matter is to be found in the Hoffman *vs.* Brooks Construction Co. decision.[3]

25 E. Washington St., Chicago, Ill.

[3] Hoffman *vs.* Brooks Constr. Co. 41 N.E.R. (2nd) 613 (May 1942).

CASE REPORTS

Unusual Case of Carcinoma of Both Lungs Associated With Lipoid Pneumonia[1]

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New York, N. Y.

A 52-year-old, single French-Canadian housemaid was admitted to the Presbyterian Hospital, New York (No. 640620) in April 1941. Her symptoms began ten months before admission with an acute upper respiratory infection which subsided in one week. Following this she had a lingering cough which persisted until admission. The cough was

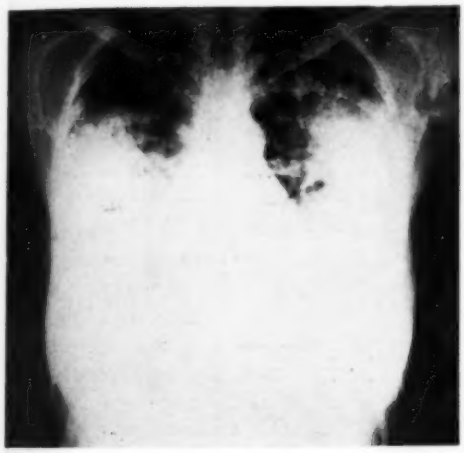

Fig. 1. Bilateral pulmonary carcinoma associated with lipoid pneumonia. The lung shadows are symmetrical and fairly homogeneous in the lower portions of the lung fields and along the lateral chest walls. In the apices and peri-hilar regions the shadows are mottled, and air-containing lung can be seen.

productive of only a small amount of whitish milky sputum at this time. Six months before admission the cough became productive of about two cupfuls daily of thin, watery, odorless sputum without blood. Three months before admission the patient began to experience dyspnea on exertion. Throughout the ten months of her present illness she lost 25 pounds and experienced several, irregularly spaced, short febrile attacks.

Ten years before admission the patient had had sinusitis, which was later recurrent and chronic.

[1] From the Department of Radiology of the Presbyterian Hospital and the College of Physicians and Surgeons of Columbia University, New York. Accepted for publication in October 1942.

Fig. 2. Bilateral pulmonary carcinoma associated with lipoid pneumonia. The air-filled tree of the trachea, main bronchi, and larger branches is well visualized on the planigraphic section. There is no evidence of a lesion involving the larger bronchi.

At the time of her first episode of sinusitis she used four bottles of oily nose drops in one week. She continued to use this material intermittently but never again in such large quantities. She habitually used mineral oil for constipation for at least fifteen years before her present illness.

On admission her temperature was 100° F. and it was not strikingly elevated at any time. Her respirations were of increased frequency, and physical examination showed her to be extremely dyspneic and cyanotic even at rest, but she was able to lie flat in bed. Physical signs suggestive of incomplete consolidation were found over the lower two-thirds of both lungs. There was no evidence of clubbed fingers, increased venous pressure, or peripheral edema.

The patient continued to produce from one to two pints daily of thin, odorless, whitish, milky, foamy sputum without blood. Many fat droplets and numerous fatty acid crystals were identified in the sputum. No tubercle bacilli or fungi were found on repeated examinations.

During her hospital stay the patient became steadily worse. There was complete failure of response to sulfadiazine. Near the end she was markedly cyanotic and dyspneic in spite of breathing pure oxygen continuously. She died on the seventeenth hospital day.

Films of the chest on admission showed a fairly dense, homogeneous shadow in the lower two-thirds of both lung fields, more extensive at the bases and along the lateral chest wall. The shadows became less dense and more mottled toward the apices. Air-containing lung could be seen only in the apices and peri-hilar regions. The lesions appeared quite symmetrical in the two lungs. Planigraphic sections showed well the air-filled tree of the trachea, stem bronchi, and larger branches. The contour was regular and there was no evidence of a lesion in the bronchial tree or of pressure or constriction from the outside. Another roentgen examination shortly before death showed no change in the lung shadows.

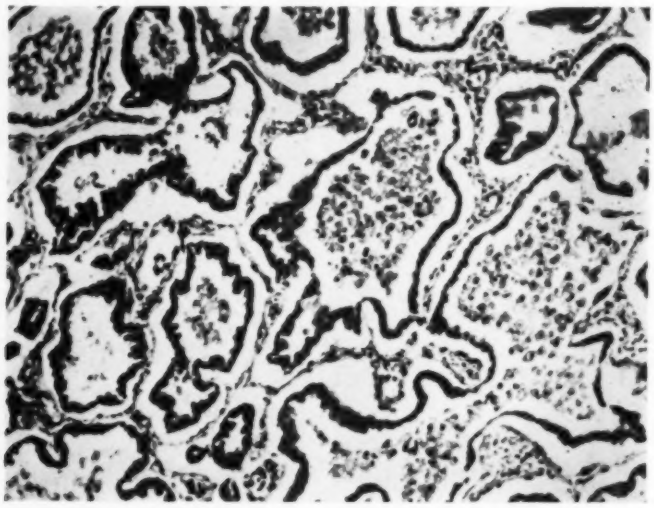

Fig. 3. Alveolar carcinoma of lung and lipoid pneumonia. Tumor cells line alveolar walls. In the darker areas the normal simple squamous alveolar lining has been replaced by pseudo-stratified cuboidal and columnar epithelium. Alveoli contain fat-laden phagocytes.

At postmortem examination (P. H. Autopsy No. 13630) the lower lobes of both lungs were found to be almost completely consolidated by confluent, lobular, pinkish-tan tumor nodules which were proved histologically to be alveolar-cell carcinoma. The right middle lobe and lower portions of the upper lobes were likewise involved. Near the apices, however, the nodules of tumor tissue were isolated and found to be scattered in normally appearing lung tissue. The tracheobronchial tree was uninvolved by disease and the tracheobronchial lymph nodes and mediastinal nodes were normal.

Microscopic examination showed the alveoli to be lined by rings of simple columnar or pseudo-stratified columnar tumor epithelium. As a result of the epithelial proliferation there were papillomatous projections into the alveoli. Few mitoses were seen. Local invasion was present and destruction of the alveolar septa was prominent. Another prominent feature of the picture was the presence of an extensive lipoid pneumonia in most of the sections. No evidence of distant metastases was found. All of the tracheobronchial and mediastinal nodes examined were negative for tumor.

Anatomical Diagnoses: Lipoid pneumonia; carcinoma of lungs; abscess of lung; fibrinopurulent pleurisy, bilateral; pyelitis cystica; myoma of uterus.

COMMENT

The long history of the use of mineral oil as nose drops and the presence of lipoid pneumonia at autopsy are of interest. Some correlation can be established between lipoid pneumonia and carcinoma arising from the epithelial cells lining the alveoli of the lung. Twort and Lyth (6) have found that several fractions of natural mineral oil readily produce primary lung tumors in mice. Shimkin (3, 4) has produced pulmonary cancers in mice resembling that found in this case by the intratracheal injection of hydrocarbons. These tumors were always nodular and arose from the alveolar epithelium, with the formation of papillary outgrowths into the alveoli. No tumors arising in bronchi

were produced. The nodular tumors were always multiple, lay in the periphery of the lung, and did not metastasize.

A somewhat similar naturally occurring disease in animals is known. Sheep, for example, are affected by a fatal pulmonary adenomatosis which has been given the name *Jagziekte*. Bonne (1) has described this disease as a condition in which the total aspect of the lung resembles that of a tumor, either an adenoma or an adenocarcinoma arising from the cells lining the alveolar sacs. Mitoses were few and metastases were never found in the nodes at the hilum. A somewhat similar disease, described by Theiler (5), occurs in horses and has been shown to be due to the eating of an oily plant. It may be that the sheep lesion is similarly caused and this is suggested by the constant finding of large collections of fat-containing mononuclear cells in the alveoli in *Jagziekte*, which have been described by Cowdry and Marsh (2).

On microscopic examination of human material from cases of lipoid pneumonia there are observed metaplasia of the squamous alveolar lining epithelium and thickening of the alveolar septa. Resultant or concomitantly occurring carcinomatous changes in the lung in man, however, must be rare.

SUMMARY

A case of bilateral alveolar carcinoma of the lung associated with lipoid pneumonia due to the inhalation of mineral oil is reported. The findings are analogous to certain experimental and naturally occurring lung tumors in animals.

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Case of Solitary Myeloma of the Skull[1]

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New York, N. Y.

Solitary myelomas of the bone are uncommon (Cutler, 1; Pasternack and Waugh, 2; Paul and Pohle, 3). Paul and Pohle in 1940 reviewed 45 cases (40 from the literature and 5 of their own). Willis (4), in 1941, added another case. The most common location of the disease was the pelvis, a vertebra, or a long bone. The skull was the site of involvement in only 5 of the 46 cases reported in the literature; 3 were in the cranial vault and 2 in the maxilla.

Mathias (5) reported the case of a 65-year-old man with a solitary myeloma of the right parietal bone. His patient, like ours, showed no Bence-Jones proteinuria. The tumor was excised and no recurrence or secondary "multiple" myelomatous lesions were observed after a period of eighteen months. Peyton (6) reported a solitary myeloma of the left parietal bone in a 38-year-old woman who complained of a painless swelling. Bence-Jones proteinuria was noted four months later, and six months after the appearance of the primary tumor roentgenographic evidence of multiple myeloma was found. Cappell and Mathers (7) presented a case of solitary myeloma of the petrous portion of the temporal bone which extended into the sphenoid. Paul raised the question, however, as to whether the tumor arose in the bone or in the otic or mastoid mucosa. Gross and Vaughan (8) and

[1] From the Department of Radiology of the College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York, N. Y. Accepted for publication in October 1942.

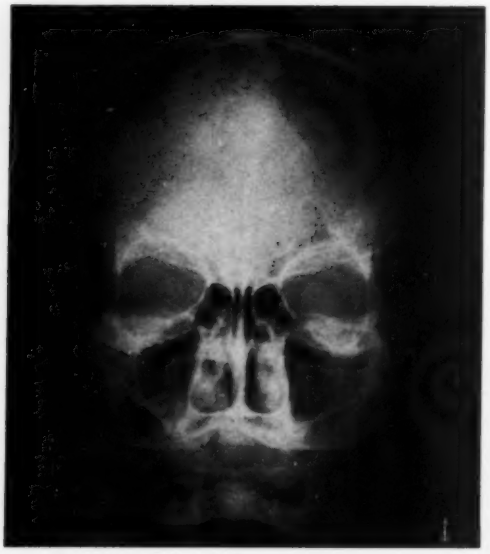

Fig. 1. Solitary myeloma of the skull. Postero-anterior roentgenogram of skull showing a large area of diminished density in the left frontal bone.

Stewart and Taylor (9) each reported a case of solitary myeloma in the maxilla, but the possibility of origin in the mucous membrane rather than in bone cannot be ruled out. The literature, therefore, contains only 2 cases in which it is certain that a solitary myeloma arose within the bone of the skull.

CASE REPORT

A 69-year-old white man was admitted to the hospital May 3, 1942, because of a swelling on the left forehead. It was painless and not tender and had been called to his attention by a friend two weeks previously. The patient recalled no injury to this area. He was thrown from a horse and fractured his left humerus five and a half years previously, but it is certain there was no head injury. This fracture healed uneventfully.

One week before admission, the patient consulted a physician. Roentgen examination at that time showed a large defect in the left frontal bone involving both inner and outer tables. No definite diagnosis was made. The patient stated he had felt better the past year than ever before. His appetite was excellent and he had gained about 10 pounds in the previous year. He never had headaches, but he had noticed a gradual failure of vision of the left eye for a period of two or three years. Two years previously he was examined by an ophthalmologist, who found mild night blindness and an incipient cataract of the left eye. There were no urinary symptoms whatever. Two years previous to admission there had been an episode of ankle edema. Complete physical examination at that time was negative. The edema disappeared and did not recur. Three years before admission, the patient had a sudden pain in the back, which lasted twenty-four hours. He was thoroughly investigated in another hospital. No evidence of organic disease was found. The pain did not recur.

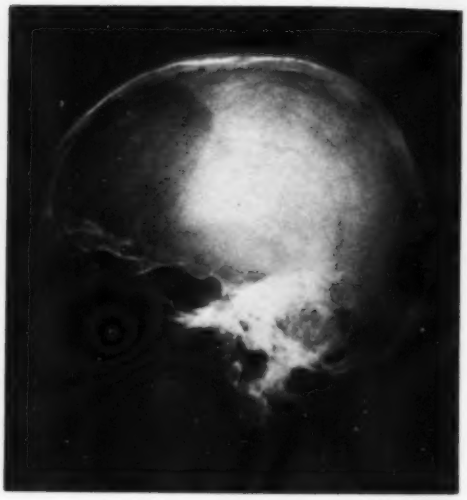

Fig. 2. Solitary myeloma of the skull. Left lateral view of the skull showing the defect in the left frontal bone extending into the parietal bone. Strands of bone cross the defect.

Physical examination was essentially negative except for a diffuse swelling of the left frontal region beginning about 2 cm. above the left eyebrow and extending well back into the hair. The swelling was soft, non-tender, non-fluctuant. A definite bone defect beneath portions of the swelling could be felt, the edges of which were irregular, sharp, and firm. This bony defect was roughly oval, measuring about 3 × 6 cm., with its greatest diameter in the anteroposterior axis. There was no discoloration over the swelling and no loss of hair in this region. Vision in the left eye was impaired. The form but not the details of objects could be distinguished. Visual fields were normal. The left lens was cloudy. The prostate was moderately enlarged and firm, with one nodule palpable in the right lobe.

Laboratory findings: The hemoglobin was 15.2 gm.; red blood cells 5,010,000; white cells 6,100 (polymorphonuclears 73 per cent; lymphocytes 21 per cent; mononuclears 3 per cent; eosinophiles 3 per cent); blood smear normal; Kline test negative. The urine was negative. No evidence of Bence-Jones proteinuria was found. The erythro-

cyte sedimentation rate was 6 mm. in one hour. The serum phosphatase was 2.7 Bodansky units per cent; serum calcium 9.5 mg. per cent; inorganic phosphorus 3.0 mg. per cent; nonprotein nitrogen 32 mg. per cent; serum acid phosphatase 3.0 G. units per cent; serum cholesterol 235 mg. per cent; serum protein 6.4; serum albumin 4.1; serum globulin 2.3.

Stereoscopic films of the chest disclosed evidence of completely healed minimal tuberculosis of both apices with bulla formation. No evidence of bone destruction could be seen in any of the ribs.

Stereoscopic films of the skull (Figs. 1 and 2) in both lateral and postero-anterior positions showed a large area of diminished density in the left side of the frontal bone extending back a short distance into the parietal bone. In the center of the involved area, both tables have apparently been destroyed, but around the periphery, one table, apparently the outer, is preserved. In two places strands of bone seem to cross the area of the defect. The margin of this area is quite well defined. The appearance is that of an expanding lesion which has destroyed bone by pressure. There is no evidence of atrophy of the sella turcica. The pineal gland is calcified and lies in its normal position.

Films were made of the entire skeleton except for the hands and feet. No evidence of bone destruction in any other area could be made out.

A biopsy was taken from the tumor through an incision along its upper margin. The tumor tissue was soft, reddish, and very vascular, "resembling thyroid tissue." It was enclosed in a definite capsule. The pathological report stated: "The tissue is composed almost exclusively of plasma cells packed in together with hardly any supporting framework. Many of the cells contain two, three, or more nuclei. Mitoses are infrequent and difficult to find. The cells are quite characteristic of plasma cells and only differ in that many of them have more than one nucleus and that the cytoplasm is quite granular." The diagnosis was myeloma of the skull.

The patient received roentgen therapy, a total of 4100 r (in air) over the tumor area in sixteen days. Roentgenographic examination of the skull six weeks from the date of admission showed no remarkable change from the previously described defect. No new rarefied areas that would suggest an extension of the disease could be seen. The patient was seen again approximately ten weeks after the date of admission. The soft tissue tumor in the left frontal region had disappeared although the bony defect in the skull was apparently unchanged to palpation. Four and one half months after admission, there was still no evidence of swelling. Films of the skull disclosed no change in the defect when compared with those taken at the time of admission. No evidence of bone repair could be made out.

As stated by Cutler, solitary myelomas are of two clinical types: those that are solitary at first, but later become multiple, and with the rare, true solitary myeloma which remains localized for four years or longer. It is possible that all multiple myelomas commence as unrecognized solitary myelomas. Yet the establishment of the diagnosis of solitary myeloma is of real value, since the solitary lesion is amenable to therapy and has a much more favorable prognosis. In our case, the period of observation is too short to determine into which of the two groups it will eventually fall.

The lack of Bence-Jones proteinuria and the normal blood protein findings in this case are of interest. Mathias' case, which after 18 months remained a solitary myeloma, showed no Bence-Jones protein. Peyton's case, which became multiple after six months, showed Bence-Jones protein two months before generalization of the disease. In Pasternack's series, only 13 per cent of the cases showed this finding at the time the solitary lesion was discovered. In 2 of 31 cases it appeared after generalization of the disease.

The diagnosis in our case could be established only by biopsy. The importance of this procedure is worthy of emphasis.

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EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

The Problem of Gastric Cancer

The general medical attitude toward gastric cancer, prior to the twentieth century, was one of extreme pessimism. This was justified, in the first place because of the lack of means of making a diagnosis in the early stages of the neoplasm, and in the second place because of the high mortality attendant on its operative removal. The opening of this century saw the beginnings of roentgenologic study of the digestive tract, which, by making possible the detection of gastric cancer in its resectable stage, was destined to revolutionize the managment of this disease. Upon surgery now devolved the responsibility of perfecting the technic of gastrectomy and thereby reducing the operative mortality. Recent reports from various surgical groups give at once an encouraging and disappointing picture and present a challenge to all those interested in the diagnosis and treatment of this serious condition.

It is generally conceded that roentgen examination is the most useful aid in the early diagnosis of cancer of the stomach. By this means it is possible not only to demonstrate the gastric lesion in nearly every case but in a high percentage actually to make a definite diagnosis of cancer. Walters, Gray, and Priestley (3), in a review of a large series of cases in which gastric resection was done, report that in 99 per cent a gastric lesion had been demonstrated roentgenologically, although 10 per cent of the lesions were originally diagnosed as gastric ulcers. In another series, Cooper (2) found the accuracy of the roentgen examination to be 86 per cent, with an additional 3.1 per cent suggestive of cancer. In 97.8 per cent of his series a gastric lesion was demonstrated. In 80 per cent of the early, resectable cases the roentgenologist made a diagnosis of cancer.

The figures quoted above demonstrate the accuracy of roentgen examination, but attention should be drawn to the fact that when *only early resectable cases* are considered the percentage falls sharply. Patients with small gastric lesions, the exact nature of which is not obvious, must be repeatedly examined until all doubt is cleared up. It is in such cases that one may expect the greatest number of surgical cures and the lowest surgical mortality.

Another weapon which is now available in the fight against cancer of the stomach is the flexible gastroscope. While exact statistics of its value are not at present available, there is increasing evidence that additional preoperative information may be gained by its use in certain ulcerative lesions the etiology of which is not clear. Its chief application is in the study of the mucosa and the margins and bed of the ulcer, but great significance should also be attached to its use in gastritis and polyposis for the detection of precancerous lesions.

Complete surgical eradication of the neoplasm is the method of choice in the treatment of cancer of the stomach. The final statistics in any series will depend upon many factors, the chief one being the stage at which a diagnosis is made.

In a statistical report from the Mayo Clinic, covering the years 1907–38, Walters, Gray, and Priestley (3) review the results obtained in 11,000 cases of gastric cancer. Resection was possible in 2,772 patients, with an average operative mortality of 16 per cent, though this latter

figure has been progressively lowered in recent years. The five-year survival rate after resection was 29 per cent, the ten-year survival rate 20 per cent, and the fifteen-year survival rate 15 per cent. Of those patients without extension of the disease or metastases, 44.7 lived five years after leaving the hospital, but of those with metastases, only 17.3 per cent survived the five-year period. Having analyzed their findings, the authors state in conclusion that in cases of persistent dyspepsia, regardless of its type, roentgenographic studies and, when necessary, supplementary gastroscopic examinations, furnish an accurate method of diagnosis. Medical treatment should not be instituted without a preliminary roentgenologic examination.

Boyce (1) in a report of gastric carcinoma seen at the Charity Hospital of Louisiana paints a much less hopeful picture and one which he believes is more representative of the general incidence of gastric carcinoma and the mortality of gastric resection. His statistics, presented graphically, show that of every 30 patients with carcinoma of the stomach who enter the Charity Hospital, only 10 can be submitted to surgery; of these 10 patients, 5 receive only palliative operations; in 3 only exploration is done; 2 have gastrectomies, and of these only 1 leaves the hospital alive. Boyce quotes statistics from the literature showing an operative mortality ranging from 30 to 58 per cent and points out that these figures represent the results of a large number of general surgeons in contrast to those of one or more highly trained in gastric surgery. He believes that the social status of the patient also has a bearing on the prognosis. Many of the patients in his series were of a low social level; most had advanced disease and were poor surgical risks.

In a study of 264 patients from the New York Hospital with proved gastric carcinoma, Cooper (2) found that in only 41 or 15.5 per cent was a diagnosis made sufficiently early for the case to be considered curable by surgical resection. The mortality directly due to resection in these cases was 9.8 per cent. In only 9 cases had resection been done more than five years previously, but of this group 4 patients were living and well, a five-year survival rate of 44.4 per cent.

In studying these statistics it is readily apparent that the failure of the surgeon is due largely to late diagnosis; that success can be attained only while the lesion is small and while the patient is still in a good physical condition. The responsibility for late diagnosis must be divided between the physician and the patient. For improvement we must look to both. The patient must be taught to consult his physician earlier in the presence of gastric symptoms. This is a difficult problem but not a hopeless one, for it is the general experience that patients of all types are gradually being seen earlier in the course of their diseases. The physician must be encouraged to make a more thorough physical examination, with laboratory tests and, above all, a complete roentgen examination, before placing the patient on medical treatment. He must realize more clearly the seriousness of gastric symptoms occurring in middle or late adult life, but at the same time must appreciate that the despondent attitude of the past is not justified in the light of our present knowledge.

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URGENT NEED OF CONSERVING X-RAY EQUIPMENT AND ACCESSORIES

Most civilian radiologists are aware that it is becoming increasingly difficult to obtain x-ray accessories, but the gravity of the situation and the necessity of taking steps to meet it are not fully appreciated. Among items in which the shortage is already severe or threatens to become so are: cassettes, intensifying screens, developing hangers, developing tanks, x-ray tubes, x-ray meters, and film driers. Most critical is the scarcity of developing hangers, which are almost unobtainable, and of intensifying screens.

Chief among causes of the condition is, of course, the tremendous demand of our armed forces. Priorities have vastly reduced the available stocks of essential materials, notably steel especially, stainless steel. To this circumstance is added the fact that many of the skilled artisans who are indispensable for the manufacture of x-ray apparatus have been inducted into the armed services, and production is correspondingly diminished.

It seems unlikely that the condition will be relieved soon or in substantial degree by governmental action, for the government must place the welfare of its fighting men above all other considerations, and all of us heartily approve of that obligation. As radiologists we must make the best of the situation by conserving the equipment we have and using it wherever it is most needed. Our past prodigality has left a wide margin for retrenchment and economy without serious loss of efficiency. Damaged equipment can be repaired. Outmoded accessories can be redeemed from private junk heaps and used again if needed. All apparatus can be handled with greater care and used only when really necessary. Equipment left behind by physicians who have joined the armed forces can be sold or loaned to civilian radiologists and put into useful service. These are only a few of the measures that we can employ, and, if we apply ourselves earnestly to this chore, we can accomplish much by efforts and sacrifices that will be very small in comparison with those made by our fighting kinsmen and colleagues.

MILITARY COMMITTEE, RADIOLOGICAL SOCIETY OF NORTH AMERICA
A. C. Christie, *Chairman*
W. Edward Chamberlain
E. P. Pendergrass
U. V. Portmann
B. R. Kirklin, *Secretary*

GEORGIA RADIOLOGICAL SOCIETY

At the annual meeting of the Georgia Radiological Society recently held in Atlanta, at the Lawson General Hospital, Dr. R. C. Pendergrass of Americus was elected President and Dr. James J. Clark of Atlanta, Secretary-Treasurer. An excellent program was furnished. Colonel Sloat, representing the Orthopedic Department of the Hospital, presented some interesting cases, Dr. Elliott Scarborough read a paper on Malignant Lesions of the Mouth, and there was a stimulating discussion of unusual and instructive cases.

VIRGINIA RADIOLOGICAL SOCIETY

The recently elected officers of the Virginia Radiological Society are: President, Wright Clarkson, M.D., of Petersburg; Vice-President, Clayton W. Eley, M.D., of Norfolk; Secretary-Treasurer, E. Latané Flanagan, M.D., of Richmond.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

FRACTURES. By PAUL B. MAGNUSON, M.D., F.A.C.S., Associate Professor of Surgery, Northwestern University Medical School, Attending Surgeon, Passavant Memorial Hospital and Wesley Memorial Hospital, Chicago. Fourth Edition, Revised. A volume of 511 pages with 317 illustrations. Published by J. B. Lippincott Company, Philadelphia, 1942. Price $5.50.

Book Reviews

INTESTINAL OBSTRUCTIONS. By OWEN H. WANGENSTEEN, B.A., M.D., PH.D., Professor of Surgery of the University of Minnesota and Surgeon-in-Chief of the University of Minnesota Hospital. Second Edition. A volume of 484 pages with 143 figures. Published by Charles C Thomas, Springfield, Illinois, 1942. Price $7.00.

This is an excellent treatise on the very important and serious clinical problem of intestinal obstruction. Beginning with the preface, right through to the last page of the last chapter, dealing with obstructions due to vascular causes, the book is full of practical suggestions regarding the manner in which intestinal obstruction disturbs the economy of the body and the diagnostic and therapeutic procedures for this most devastating human ailment.

The author very wisely has divided his material into four parts, physiological and clinical considerations; general diagnostic considerations; the management of acute intestinal obstruction; the special obstructions.

Sixty pages (Chapter I) are devoted to physiological and clinical considerations, covering the effects of distention, the character and source of distention, the manifestations of distention upon the bowel wall, and the systemic effects of distention. Absorption in obstruction, the significance of the blood loss factor in strangulating obstructions, and the nature of the toxemia associated with obstruction are also discussed.

Although it is stated that no direct and unequivocal answer has been obtained for the question of lethal factors in obstruction, the author's opinion seems to be that, apart from the loss of fluids and electrolytes, which is of serious consequence, the chief effects of obstruction are mechanical and concern intra-enteric pressure as related to the absorption and viability of the bowel wall. When the viability of the wall has become impaired, then permeation by bacteria and other deadly agents occurs, but this is a secondary rather than a primary phenomenon.

General diagnostic considerations are taken up in two chapters, covering 41 pages. One chapter deals with diagnostic methods in acute abdominal disorders, and the other with the recognition of obstruction. The latter discusses, first, the methods of determining that obstruction exists, second, the localization of the obstructing lesion, determining whether obstruction is partial or complete, and finally, the mechanism of the obstruction.

Seven chapters, 140 pages, are devoted to the very important matter of the management of acute intestinal obstruction. Chapter IV discusses guiding principles in the treatment of acute abdominal lesions. Chapter V details the important supportive measures, namely, the administration of physiologic solution of sodium chloride, blood and plasma transfusions, and the inhalation of oxygen in high concentrations. In Chapter VI decompression by application of suction through duodenal tubes is outlined. Indications for this conservative method of treatment, its technic, and shortcomings are explained. In Chapter VII operative procedures, preoperative preparation, and choice of anesthesia are outlined. A special chapter (VIII) is devoted to the closed aseptic resection. Postoperative treatment is considered in Chapter IX, and mortality in Chapter X.

Fifteen chapters, consisting of 215 pages, are devoted to a discussion of obstruction due to congenital atresia of the intestine, the imperforate anus, tumors and strictures of the bowel wall, obturation, obstruction, fecal obstruction as in megacolon, compression of the bowel by extrinsic conditions such as pelvic lesions, adhesions and bands, external hernia, internal hernia, volvulus, intussusception, errors in development of the intestine, inhibition (paralytic) ileus, spastic ileus, and obstruction due to vascular causes.

Any practitioner of medicine may be proud to have this book in his reference library. Every teacher of medicine should have it available as a textbook, as it contains the most up-to-date information on the subject and will prove a source of sound instruction for the student. In addition, it is written in an interesting, almost fascinating manner.

THE 1941 YEAR BOOK OF RADIOLOGY. Diagnosis edited by CHARLES A. WATERS, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital, and WHITMER B. FIROR, M.D., Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. Therapeutics edited by IRA I. KAPLAN, B.Sc., M.D., Director, Radiation Therapy Department, Bellevue Hospital, New York City; Associate Radiologist, Lenox Hill Hospital, New York City; Clinical Professor of Surgery, New York University Medical College. 496 pages and 496 illustrations. Published by The Year Book Publishers, Inc., Chicago, Ill., 1942. Price $5.00.

The latest Year Book of Radiology, the eleventh of this useful series, appears under the continued editorship of Dr. Charles A. Waters, Dr. Whitmer B. Firor, and Dr. Ira I. Kaplan, though an introductory note informs the reader that Doctor Firor, at the time of publication, was already in Australia with the armed forces. Though it bears the date 1942, only publications of the first half of the year are reviewed, the period covered apparently running from the middle of 1941 to the middle of 1942, with the inclusion of a few pertinent papers of earlier date.

The treatment of the material is much the same as in former years. The articles reviewed are adequately abstracted and well illustrated. There is, as is to be expected, a much greater preponderance of American papers—both North and South—than in former years, though the British and Scandinavian literature is represented. Indexes of subjects and authors increase the value of the work.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse, N. Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association.—Secretary, J. T. Murphy, M.D., 421 Michigan St., Toledo, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary-Treasurer, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Joseph D. Coate, M.D., 434 Thirtieth St., Oakland.

Los Angeles County Medical Association, Radiological Section.—Secretary, Donald R. Laing, M.D., 65 N. Madison Ave., Pasadena. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, Earl R. Miller, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School); second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Edward J. Meister, M.D., 366 Metropolitan Bldg. Meetings third Friday of each month at the Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Acting Secretary, Walter A. Weed, M.D., 204 Exchange Building, Orlando.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, James J. Clark, M.D., 478 Peachtree St., N. E., Atlanta. Meetings twice annually, in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Warren W. Furey, M.D., 6844 S. Oglesby Ave. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Fay H. Squire, M.D., 1753 W. Congress St., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Sydney E. Johnson, M.D., Louisville City Hospital, Louisville. Meeting annually in Louisville, third Saturday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary-Treasurer, W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, E. M. Shebesta, M.D., 1429 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, Arthur B. Smith, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of each month except June, July, August, and September, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, F. L. Simonds, M.D., 1216 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Maurice Pomeranz, M.D., 1120 Park Ave., New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., 707 Race St., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport. The Society meets annually.

The Philadelphia Roentgen Ray Society.—Secretary, Robert P. Barden, M.D., 3400 Spruce St., Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Reuben G. Alley, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston Meeting in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, Herman Klapproth M.D., Sherman.

VIRGINIA

Virginia Radiological Society.—Secretary E. Latané Flanagan, M.D., 215 Medical Arts Bldg., Richmond.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russell F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. D. Irvine, M.D., 540 Tegler Bldg., Edmonton, Alberta.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

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THE HEAD AND NECK

Epidermoid, Dermoid and Teratomatous Tumors of the Central Nervous System. W. T. Peyton and A. B. Baker. Arch. Neurol. & Psychiat. **47**:890–917, June 1942.

In an excellent article the author reports on 14 congenital tumors involving the central nervous system. These include 9 epidermoids, of which 6 were intracranial, 2 intradiploic, and one was located in the spinal canal. Only one dermoid cyst was encountered in the intracranial cavity. The series includes, also, 4 teratomas, 2 intracranial and 2 within the spinal canal. Of the 6 intracranial epidermoids, 4 contained sufficient calcium to be recognized in the roentgenogram.

The authors describe the roentgen appearance of these tumors both within the diploe of the cranial vault and also when they occur within a lateral ventricle. The intraventricular epidermoid presents an encephalographic picture from which it is possible not only to locate the tumor but also to recognize its nature. The characteristic feature is ventricular displacement, with replacement of most of the normal ventricular gas by a more extensive area of irregular collections or streaks of air. Roentgenograms of the intradiploic epidermoid taken so that the greatest diameter of the defect is shown reveal a dense clear-cut scalloped margin of eburnated bone.

The article includes a lengthy review of the pertinent literature and the clinical and histologic aspects of these tumors. CORNELIUS G. DYKE, M.D.

Ganglion Cell Tumor (Ganglioglioma) in the Third Ventricle: Operative Removal with Clinical Recovery. F. M. Anderson and L. J. Adelstein. Arch. Surg. **45**: 129–139, July 1942.

Ganglion-cell tumors of the brain are unusual. The most common location of this tumor in the brain is the floor of the third ventricle; the next most common, the temporal lobe. The tumor is relatively benign; the more adult form, the ganglioglioma, is generally quite chronic, while the embryonic form, the ganglioneuroblastoma, runs an acute course. The neoplasm is generally, but not always, sharply demarcated from the brain substance and has little tendency toward invasion.

The tumor is usually gray, but may contain areas of yellow pigmentation and hemorrhage; it may be cystic or show central necrosis. The striking feature microscopically is the presence of ganglion cells of various stages of maturity.

Surgical removal, particularly in the third ventricle, has proved difficult. Indeed, there is no previous record of the successful removal of a ganglion-cell tumor from this site.

Third ventricle tumors produce a fairly constant symptom complex, consisting of hypersomnia; psychic disturbances; vegetative symptoms, including derangements of heat regulation, adiposity, genital dystrophy, and circulatory dysfunction; thalamic symptoms, as painful hypesthesia and central pain; pyramidal and cerebellar signs.

A case in which successful removal of a ganglion-cell tumor of the third ventricle was effected is reported. The patient was a nine-year-old boy with a history of gradual impairment of vision for three years, with progressive development of headache, somnolence, and vomiting. Ventriculography revealed bilateral symmetric internal hydrocephalus and complete absence of air in the third ventricle. A right frontal craniotomy was done and a large ganglioma was found completely filling the anterior portion of the ventricle. It was completely removed and the patient made a good recovery, though vision was not improved. LEWIS G. JACOBS, M.D.

Diverticula of the Lateral Ventricles Extending into the Cerebellar Fossa. A. E. Childe and F. L. McNaughton. Arch. Neurol. & Psychiat. **47**: 768–778, May 1942.

The authors describe in detail a case of spongioblastoma polare arising from the hypothalamic region of the brain. The patient had advanced internal hydrocephalus with associated diverticula of the median portion of the atrium of the lateral ventricle. On one side the protrusion of the lateral ventricle through the tentorial incisure into the cerebellar fossa was sufficiently large to produce a cavity beneath the tentorium quite similar in appearance on the roentgenogram to an enlarged fourth ventricle. This led to a correct localization of the tumor, but it was only at necropsy that the actual condition was ascertained. A photograph of the left half of the brain after mid-sagittal section shows the position of the protrusions within the subarachnoid space, occupying roughly the central portion of the cisterna ambiens.

A number of similar cases are cited and references to the literature are given. It is suggested that these diverticula are the result of long-continued high intracranial pressure, with resultant internal hydrocephalus and the development of a weak point in the floor of the lateral ventricle overlying the incisura tentorii. CORNELIUS G. DYKE, M.D.

An Encephalographic Ratio for Estimating Ventricular Enlargement and Cerebral Atrophy. W. A. Evans, Jr. Arch. Neurol. & Psychiat. **47**: 931–937, June 1942.

The author describes a method of determining the size of the lateral ventricles of the brain by establishing the ratio of the transverse diameter of the anterior horn to the internal diameter of the skull, measured in encephalograms made in the horizontal anteroposterior position. The average value of the ratio for a "normal" series of encephalograms was found to be 0.23 with extreme values of 0.16 and 0.29. A significant correlation was found between the size of the ventricles and the size of the skull, the ratio having the same average value for small and large skulls and for the skulls of infants, children, and adults. The normal ratio varies for the most part between 0.20 and 0.25. Values above 0.30 are indicative of ventricular enlargement. CORNELIUS G. DYKE, M.D.

Spontaneous Atlantoaxial Dislocations: Possible Relation to Deformity of Spine. J. H. Hess, S. M. Abelson, and I. P. Bronstein. Am. J. Dis. Child. **64**: 51–54, July 1942.

A 5-year follow-up study of a patient with an unreduced spontaneous unilateral rotary atlantoaxial dis-

location is presented. The patient was first seen at the age of 7 years when the diagnosis was made and treatment refused.

Examination at the age of 12 years revealed moderate asymmetry of the face, elevation of the left shoulder, and left kyphoscoliosis. The head was inclined to the left and the chin turned to the right. The spine of the axis was felt to the left of the mid-line, and rotation of the head to the left was limited.

The relation of this lesion to deformities of the spine is suggested, with the further suggestion that its presence should be looked for in cases of unexplained postural kyphosis and scoliosis.

GEORGE M. WYATT, M.D.

THE CHEST

Actinomycosis of the Lung. M. T. Cockburn. M. J. Australia **2:** 7, July 4, 1942.

A case of actinomycosis of the lung is presented because of its rarity and the difficulty in making a diagnosis.

A Polish officer of 41 years entered a British hospital on July 23, 1941, complaining of malaise and a dry cough associated with fever of ten weeks' duration. Pain in the left chest was aggravated by coughing. The patient had been ill a year previously with what had been described as a pneumonia involving the bases of both lungs.

Dullness to percussion and diminished breath sounds were elicited over the upper left lobe. There was clubbing of the fingers and toes. Examination of the sputum was essentially negative. The blood count was normal. The blood sedimentation rate was 109 mm. in the first hour. Roentgenograms of the chest showed an opacity of the middle zone of the left lung which was interpreted as an interlobar effusion. A diagnosis of pulmonary tuberculosis with effusion was made. During ten weeks in the hospital there was little change in the condition except for disappearance of fever.

In October 1941 the patient was transferred to the Sixth Australian Hospital. His physique was poor and he had a severe cough with variable amounts of sputum, which sometimes was offensive and once was blood-stained. Roentgenograms showed the left lung opacity essentially unchanged, and the possibility of consolidation rather than effusion was suggested. On the basis of a weak Kline test antisyphilitic treatment was instituted, but without favorable results.

About the middle of November 1941 a roentgenogram of the chest showed that the area of opacity in the left lung was more extensive. A diagnosis of bronchogenic carcinoma was made but was not substantiated by lipiodol studies. After this procedure the patient raised more sputum and his fever was as, high as 102°. Aspiration of the left chest on Nov. 25 did not produce any significant evidence. A Kline test and sputum examination on Dec. 1 were negative.

On Dec. 8 a thoracotomy was done and a loculated abscess cavity was drained. Six ounces of thick, foul pus were evacuated and examination of the material showed "organisms morphologically indistinguishable from those of actinomycosis." The patient died forty-eight hours after the operation. Autopsy revealed an abscess cavity 3 × 5 cm. in the upper lobe of the left lung. The inflammatory process about the cavity was of solid consistence and contained numerous yellow areas. Microscopic examination showed lipoid pneumonia.

DONALD R. LAING, M.D.

Coccidioidal Granuloma (Coccidioidomycosis): Its Incidence in Man and Animals and Its Diagnosis in Animals. G. W. Stiles and C. L Davis. J. A. M. A. **119:** 765–769, July 4, 1942.

A highly fatal disease in man, known as coccidioidal granuloma, was recognized for many years in central California, while in the same locality there existed a non-fatal influenza-like disease known locally as "valley fever," "desert fever," "desert rheumatism," or "San Joaquin Valley fever." In 1936 Dickson and Gifford showed that the two maladies were caused by the same organism, *Coccidioides immitis*.

Valley fever resembles influenza in its initial stage. In about 5 per cent of the cases it is followed in a few days by the eruptive phase of erythema nodosum; less frequently by erythema multiforme. The mortality is negligible. *Coccidioidal granuloma* is a chronic, progressive, highly fatal fungus disease affecting the lungs, skin, lymph nodes, bones, meninges, thoracic viscera, and other body tissues. The infection in cattle has thus far been confined to the thoracic lymph nodes and the lungs. In man coccidioidomycosis closely mimics tuberculosis and frequently may be mistaken for that disease. Recovery of the fungus from the sputum or body tissues should verify the diagnosis.

Pulmonary infection may be acquired by inhalation of the vegetative phase of dust-laden chlamydospores. The vegetative form of the fungus is believed to exist more frequently during rainy periods in arid regions where the winters are relatively warm and summers are hot, dry, and dusty. Abrasion of the skin may be a route of infection, and in rare instances the disease may be acquired by way of the gastro-intestinal tract. Man-to-man and animal-to-man infection probably does not occur.

The great majority of cases of coccidioidal granuloma occur in California, originating in the southern San Joaquin Valley, but its appearance both in man and animals from other localities indicates that the malady is either spreading or has not heretofore been recognized. Cases have occurred in Arizona, Colorado, Illinois, Kansas, Missouri, Nebraska, New Mexico, Pennsylvania, South Carolina, Texas, and Washington. Alaska, Tennessee, Louisiana, and Hawaii have also reported the occurrence of the disease.

The veterinary phase of the problem has its place in relation to public health and animal welfare. Six species of rodents trapped in the vicinity of San Carlos, Arizona, have been found to have the disease. Farness reports cases in dogs and cats at Tucson, Arizona. Evidence is presented that a variant of *Coccidioides immitis* is present in the Phoenix, Arizona, district, that it affects sheep in particular, and that it produces a non-fatal, usually undiagnosed illness in human subjects.

During the past ten years 78 positive cases of coccidioidal infection in bovines were diagnosed in the laboratory of the Denver Bureau of Animal Industry. These originated as follows: from California 62, from Arizona and Texas 5 each, from Old Mexico 4, from Colorado and New Mexico 1 case each. These definitely diagnosed cases represent many additional cases in animals sent for slaughter, since only representative samples

from a lot are sent to the laboratory for examination. A summary of the data now at hand shows a total of 116 definitely diagnosed cases of bovine coccidioidal granuloma in the United States. It is probable, however, that many more cases in cattle have escaped identification or were not submitted for laboratory confirmation.

Cattle affected with coccidioidal granuloma show no clinical symptoms and the lesions thus far observed have been confined to the thoracic lymph nodes and the lungs and are detected only when the animals come to slaughter. Grossly the lesions may be confused with tuberculosis, actinomycosis, actinobacillosis, or abscesses due to *Corynebacterium pyogenes*. The 78 bovine cases reported in this article were diagnosed in the Denver laboratory either by the demonstration of spherules in press preparations of the purulent contents, positive cultures of *Coccidioides immitis* being obtained, or by microscopic sections.

Microscopic study of sections of the lesions stained with hematoxylin-eosin show a granulomatous process consisting of connective tissue, blood vessels, plasma cells, mononuclear and polymorphonuclear leukocytes, a few eosinophile and giant cells. Scattered throughout the tissue are variable numbers of double-contoured spherules, the majority of which have been taken up by giant cells. In some fields the cellular reaction mimics a tubercle.

CLARENCE E. WEAVER, M.D.

Pleuropulmonary Tularemia: Report of a Case with Recovery. J. O. Finney. South. M. J. **35:** 660–663, July 1942.

Verbrycke was the first to demonstrate pulmonary lesions in tularemia at autopsy, in 1924 (J. A. M. A. **82:** 1577, 1924). *Pasteurella tularensis* was recovered from the sputum by Bunker and Smith in 1928 (U. S. Nav. M. Bull. **26:** 901, 1928). The condition is uncommon.

The author's patient, a 26-year-old white male textile worker, was admitted to the hospital in delirium. His illness had begun suddenly ten days earlier, with severe chills and high fever. Chest pain and cough developed one week after onset. The white blood count was 16,000. Aspirated pleural fluid showed specific gravity of 1.020, with lymphocytes predominating. Blood agglutination was positive for *P. tularensis*. Roentgenograms of the chest showed an exudative pleuro-pneumonic process. Under treatment with large doses of sulfanilamide and sulfathiazole the patient made an uneventful recovery.

Clinically and roentgenologically tularemic pneumonia has no unique characteristics.

MAX MASS, M.D.

Hydatidosis of the Lung. J. Arce. Surg., Gynec. & Obst. **75:** 67–73, July 1942.

The author reports in detail the course of a patient with hydatidosis, or echinococcosis, of both lungs—a large cyst in the left lung and a smaller one in the right. The cyst in the left lung was evacuated and the remaining walls were thoroughly cleansed. A year later, an attempt was made to remove the cyst in the right lung by an extrapleural approach. A right pleural effusion resulted. Chest studies at the time showed several small rounded shadows within the residual cavity in the left lung. Subsequent roentgenograms, thirty months after the first operation, showed the cavity completely replaced by the typical shadow of another hydatid cyst. The author assumed, and proved by subsequent operation, that fertile scolices had remained in the residual cavity and had grown to form a second hydatid cyst at the original site.

A second somewhat similar case is cited and it is pointed out that the live—and therefore fertile—hydatid elements (scolices, hydatid vesicles) are capable of becoming grafted on human tissues and, without undergoing the *Taenia* stage, of giving rise to a new cyst. This has been demonstrated experimentally, and clinical observations have shown recurrences in operative scars following removal of hydatid cysts from liver, lung, and other locations.

The two cases reported here are, as far as the author knows, the only ones on record of grafts in the residual cavity following operation. He believes that this type of recurrence is favored by the Posadas method—evacuation of the cyst and suture without drainage—and recommends that, in cases where this method must be employed, the interior of the cavity be thoroughly cleansed with ether before closing the wound.

IVAN J. MILLER, M.D.

An Acute Respiratory Infection Resembling So-Called Acute Pneumonitis: Report of 40 Cases. L. B. Duggan and W. L. Powers. U. S. Nav. M. Bull. **40:** 651–659, July 1942.

This is a study of 40 cases of an acute infectious disease of the respiratory tract recently observed in a U. S. Naval Hospital. The cases reported were of insidious onset, with minimal respiratory and constitutional symptoms and a slightly elevated leukocyte count. Roentgen studies of the chest showed a small area of increased density most often at the base or hilus of one lung. The disease is believed to be of possible virus origin. The response to the sulfonamides was less favorable than in the usual pneumococcic infection.

Transitory Pulmonary Infiltrations Mistaken for Tuberculosis, with a Report of Five Cases. A. A. Karan and E. Singer. Ann. Int. Med. **17:** 106–124, July 1942.

Five cases are recorded in which chest roentgenograms showed shadows so closely resembling tuberculous infiltrations that a diagnosis of tuberculosis was made, though it was subsequently found that the condition was non-tuberculous. Two of the cases proved to be bronchopneumonia probably due to a filtrable virus. The roentgenograms at the onset of the illness, the symptoms, and the blood picture were strongly suggestive of the exudative type of tuberculosis, but serial roentgen study showed rapid resolution of the pulmonary infiltration, and this, with failure to find tubercle bacilli in the sputum, disproved the original diagnosis.

In 2 instances the infiltration was of the type described by Löffler, associated with eosinophilia (Schweiz. med. Wchnschr. **66:**1069, 1936), though the symptoms were more severe and clearing of the lungs was less rapid than in the usual Löffler case. In the remaining patient the diagnosis was not definitely established but the original roentgen findings were attributed to lobular atelectasis with beginning pulmonary necrosis as a sequence of bronchial obstruction.

The authors state in conclusion that reliance on a single chest roentgenogram for diagnosis frequently

leads to error, and that, when tubercle bacilli cannot be found in the sputum or aspirated gastric contents by any method of examination, including cultures and guinea-pig inoculation, it is extremely unlikely that the bronchopulmonary disease is tuberculous.

J. A. L. McCULLOUGH, M.D.

Management of the Minimal Tuberculous Lesion. A. L. Krueger, B. P. Potter, and A. E. Jaffin. Am. Rev. Tuberc. **46:** 50–58, July 1942.

Because there has been some controversy as to the proper method of treating the minimal tuberculous lesion the authors reviewed the records and x-ray films of 185 cases belonging in this category. Analysis of the results shows that arrest of disease was accomplished by bed rest as an initial procedure in 78 per cent of the series. The results of treatment were more satisfactory in those patients treated in the hospital or sanitarium than in those treated in the clinic or at home, since twice as many recurrences were encountered in the latter group. Collapse therapy is recommended in this type of patient only when progression of the lesion occurs, when tubercle bacilli are recovered from the sputum and fail to disappear after a liberal period of bed rest, or when hemoptysis is present. L. W. PAUL, M.D.

Diabetes Mellitus and Tuberculosis. J. V. Skavlem, C. A. Castle, and F. R. Moore. Dis. of Chest. **8:** 209–212, July 1942.

The authors report a series of 3 cases emphasizing the increased severity of diabetes when tuberculosis supervenes, the occurrence of tuberculosis in diabetic patients after coma, the necessity of frequent physical examination and roentgen study of the chest in diabetics. Statistics are quoted showing that pulmonary tuberculosis occurs two to three times as often in persons with diabetes mellitus as it does in the general population.

WILLIAM H. GILLENTINE, M.D.

Some Notes on Cystic Disease of the Lungs, with a Report of One Case. W. R. Stanford and B. C. Nalle, Jr. Ann. Int. Med. **17:** 65–77, July 1942.

The authors report a case of cystic disease of the lungs, with clinical and pathological findings, illustrated by reproductions of roentgenograms and photographs of pathological specimens. Special emphasis is placed on the difficulty of differentiating between congenital cystic disease, acquired cystic disease, and extensive emphysema. The case reported was roentgenologically typical of that group which has been diagnosed as congenital cystic disease of the lung, but as the patient, a man of 34, had experienced no symptoms until four years previously, it was suggested that the condition was probably acquired. Multiple emphysematous blebs were present on the surface of both lungs and cyst-like structures were found also in the lung substance.

Following their case report the authors give a brief résumé of the pathogenesis and morbid anatomy of the condition. The cysts are of two types: fluid cysts and air cysts, the latter being either expansile or non-expansile. The clinical diagnosis is almost wholly dependent upon roentgenology. Among procedures which may be of help in making the diagnosis are lung mapping with lipiodol and induced pneumothorax. The latter, by pushing the cyst away from the chest wall, may make possible a differentiation from a spontaneous pneumothorax. The fluid cysts offer much more difficulty from a diagnostic standpoint than the air cysts. When a fluid cyst has ruptured into a bronchus the patient often gives a history of spitting up milky or albuminous fluid.

Treatment is dependent upon the size, number, location, and type of cysts, the presence or absence of infection, and the severity of the symptoms. The authors mention various procedures that have been suggested but add that, if enough lung units are destroyed, there is no surgical or medical procedure that will do any good.

J. A. L. McCULLOUGH, M.D.

Posturing in Bronchography. F. D. Hart. Brit. M. J. **2:** 7–8, July 4, 1942.

The author in opening his article makes the pointed statement that roentgenograms following bronchography are too often useless on account of the unfilled areas present. He sets forth the principle that the normal as well as the abnormal areas should be demonstrated.

The cricothyroid injection method is described but this is considered optional. The essential feature is to demonstrate each lobe of both lungs. With the two-stage method 16 c.c. of oil are used in each lung, the interval between the two sides being seven to ten days. When the one-stage method is used less oil is necessary. The difficulty incurred here lies in the necessity of demonstrating all of the regions before the oil becomes too viscid. The various postural maneuvers essential for complete distribution of lipiodol in the bronchi are described. Q. B. CORAY, M.D.

Angiocardiographic Demonstration of an Arteriovenous Fistula. M. F. Steinberg, A. Grishman, and M. L. Sussman. Surg., Gynec. & Obst. **75:** 93–96, July 1942.

The authors present a case with typical clinical evidence of arteriovenous fistula in the left upper thorax or axilla. By the angiocardiographic technic, consisting in the injection of 30 c.c. of 70 per cent diodrast into an antecubital vein, followed by serial roentgen exposures, the site and extent of the fistula were demonstrated.

The first series of roentgenograms, made following the injection of the left antecubital vein, showed an enlarged left axillary vein which, after emptying, filled again when the dye returned from the heart. Interlacing vascular channels about the head of the humerus were demonstrated. The simultaneous demonstration of both the axillary vein and artery indicated that the fistulous opening must be at or above their origins, presumably in the third portion of the subclavian artery. Revisualization of the vessels in the left axilla after a similar injection into the antecubital vein on the uninvolved side was in accord with this location, which was confirmed at operation.

Double ligation of the left axillary artery and vein failed to change the clinical picture and it was not until ligation of the left subclavian artery that the symptoms disappeared. Subsequent gangrene of the left wrist and hand necessitated partial amputation.

Angiocardiography is recommended as a simple, effective procedure for the precise localization of arteriovenous fistulas involving large vessels near the heart.

IVAN J. MILLER, M.D.

THE DIGESTIVE TRACT

A Clinical Roentgenological Review of the Literature for 1941, Pertaining to the Digestive Tract. M. Feldman. Am. J. Digest. Dis. **9:** 211–220, July 1942.

The author's introductory note indicates the nature and scope of this review.

"A review of the available 1941 literature with a brief appraisal of what is valuable pertaining to the clinical roentgenological aspects of the digestive tract is summarized. It is an almost impossible task to review every medical periodical that has been published during the year; however, nearly all of the outstanding contributions in the important journals were reviewed and the major advances are herewith recorded."

One hundred and sixty-six contributions are covered and are listed in the bibliography.

Note on the Mechanism of Deglutition. A. R. Thomas. Brit. J. Radiol. **15:** 209–210, July 1942.

A patient was discovered who possessed the entertaining talent of swallowing while standing on his head, a talent which he was accustomed to use to obtain free drinks. He obligingly drank some barium while inverted and permitted studies of his swallowing function in this position. The appearance was identical with that presented when the patient was right side up. Apparently, then, gravity was of little importance. The absence of peristalsis was conspicuous. This leads the observer to suspect that the suction theory of Barclay and Mukherji is possibly of fundamental importance in deglutition. SYDNEY J. HAWLEY, M.D.

Rectal Malignant Tumor in Childhood: Report of Two Cases. H. E. Bacon, F. D. Wolfe, and R. A. Archambault. Am. J. Dis. Child. **64:** 70–79, July 1942.

The cases of two boys, each with a malignant tumor of the rectum, are reported.

The first patient, aged 3 years 8 months, had a large reticulum-cell sarcoma which produced constipation and urinary obstruction. This patient died with local recurrence and pulmonary metastases nineteen months after operation and local irradiation.

The second patient, aged 4 years 7 months, had a small polypoid adenocarcinoma which caused bleeding and protrusion. This patient is living and clinically free of neoplastic disease five years after surgical removal of the tumor.

A few authentic cases of malignant tumor of the anus, rectum, or sigmoid colon occurring before the age of seventeen have been recorded. Malignant tumor in childhood, as proved by these cases and the 2 reported here, is not rare. It should always be suspected.

GEORGE M. WYATT, M.D.

THE PANCREAS

Case of Progressive Calcification of the Pancreas Secondary to Chronic Relapsing Pancreatitis. H. C. R. Darling. M. J. Australia **2:** 7–8, July 4, 1942.

A single woman of thirty-nine years had intermittent attacks of upper abdominal pain over a period of ten years. The attacks lasted two to four weeks and occurred every six to twelve months. An appendectomy was performed in March 1932, but in July 1932 the pain recurred. There were tenderness and rigidity of the upper right rectus muscle, and an indefinite mass could be felt deep in this area. X-ray examination of the upper gastro-intestinal tract was negative except for some evidences of duodenal irritability.

The symptoms again returned in January 1933, and a roentgenogram now showed scattered calcified areas in the pancreas. An exploratory laparotomy revealed a diffuse induration and enlargement of the pancreas. The gallbladder was normal. An x-ray examination in August 1933 showed more and larger calcifications in the pancreas, and the attacks continued during the next seven years. In February 1942 the patient was again examined and slight rigidity of the upper right rectus muscle was noted with deep tenderness above and to the right of the umbilicus. Cholecystography revealed a satisfactory function of the gallbladder. No mention is made of x-ray examination of the pancreas at this time. DONALD R. LAING, M.D.

SUBPHRENIC ABSCESS

Subphrenic Abscess with Bronchial Fistula. J. Head and T. R. Hudson. Surg., Gynec. & Obst. **75:** 54–60, July 1942.

Hepatic, perinephritic, and subdiaphragmatic abscesses frequently perforate the diaphragm and are evacuated through the bronchi. A few patients are cured by such spontaneous drainage; others succumb to pulmonary or pleural infection; in still others the condition becomes chronic and the patient is left with a persistent or intermittent productive cough.

A pathological paradox exists in this condition, in that, while collections of pus in the upper abdomen frequently burrow upward through the diaphragm, similar collections in the thorax rarely extend down into the abdomen. Thoracic symptoms are often the first manifestation of disease actually originating in the upper abdomen.

The clinical picture of perforation of a subdiaphragmatic abscess is furnished by a patient with signs and symptoms of encapsulated pus suddenly coughing up or expectorating a large quantity of pus. If he survives sudden death from drowning in his own pus or from acute bronchopneumonia, he is benefited by evacuation of the pus. Spontaneous cure is rare. If the sinus tract becomes occluded, symptoms recur.

The authors believe the roentgenogram is next to the history in diagnostic importance. The most characteristic roentgen finding is elevation of the diaphragm with air and a fluid level beneath it. Neither is invariably present. Findings in the thorax vary greatly. Empyema may be produced, as well as bronchial fistula. In acute cases there may be extensive bronchopneumonia of the lower lobe on the affected side; in chronic cases, chronic "pneumonitis" may be present in one or both lungs. Occasionally, pulmonary and pleural findings are almost entirely absent, in which event bronchography must be used to rule out bronchiectasis when marked bronchorrhea is present. The importance of serial roentgenograms is stressed.

Roentgenograms taken in the upright position after diagnostic pneumoperitoneum are of great value in diagnosis. If subphrenic abscess is present, the smooth under surface of the diaphragm on the affected side will not be demonstrable. The procedure is deemed safe.

Exploratory aspiration of the acute unperforated subphrenic abscess is dangerous. The chance of soiling

the pleura, with resulting empyema, is great. In the chronic abscess that has perforated and in which the pleura is adherent, aspiration can be done safely.

Other writers are quoted concerning prognosis. The presence of thoracic complications increases the mortality rate to 50 per cent as compared with 16 per cent in uncomplicated cases.

The treatment of subphrenic abscess with bronchial fistula is the same as that of uncomplicated cases, namely, incision and drainage. Three cases are presented. IVAN J. MILLER, M.D.

THE SPLEEN

Gaucher's Disease: Report of Case. H. A. Reisman and D. W. Utz. Arch. Pediat. **59:** 446–457, July 1942.

Since the original description of Gaucher's disease in 1882, approximately 160 cases have appeared in the literature. Gaucher characterized it as a "primary idiopathic hypertrophy of the spleen"; in 1907 Marchand advanced the theory that a foreign material deposited in the reticular cells of the reticulo-endothelial system constituted the etiologic basis for the disease; Mandelbaum and Downey, in 1916, concluded that it represented a disturbance in lipoid metabolism, and further demonstrated the evolution of the Gaucher cell from the reticular cell of the reticulo-endothelial system. In 1924 Epstein (Biochem. Ztschr. **145:** 398, 1924) and Lieb (Ztschr. f. physiol. Chem. **140:** 305, 1924) found that chemically the substance present in the Gaucher cells is a cerebroside called kerasin.

The classic description of the disease emphasizes as the most constant findings splenomegaly, secondary anemia, and leukopenia. The liver is frequently enlarged and the superficial lymph nodes may be increased in size. A wedge-shaped thickening of the conjunctiva and brownish pigmentation of the skin may occur. Some cases manifest a hemorrhagic diathesis. Osteoporotic changes in the skeleton may be in evidence. The differential count of the white blood cells shows nothing distinctive; the blood lipoids do not vary greatly from the normal.

The disease shows a distinct predilection for Jewish females in the first decade of life. In differential diagnosis Niemann-Pick disease offers the greatest difficulty.

The authors report a case, showing one reproduction of an x-ray film, an anteroposterior view of the lumbodorsal spine, indicating compression of a vertebra. Radiographic studies of the skull and long bones were in this case essentially negative. No Gaucher cells were obtained by sternal aspiration, but splenic puncture yielded large cells with double nuclei and foamy cytoplasm, highly suggestive of Gaucher's disease. Diagnosis was established pathologically after splenectomy. PERCY J. DELANO, M.D.

THE SKELETAL SYSTEM

Study of Osteoporosis by Means of Controlled X-Rays of the Bones: Part I. E. L. Gardner. Minnesota Med. **25:** 557–558, July 1942. **Part II.** R. S. Ylvisaker and E. L. Gardner. Minnesota Med. **25:** 625–628, August 1942.

In 1933 Gardner called attention to a group of patients with gastro-intestinal complaints who had a definite osteoporosis of the bones (hand and wrist), when compared with normal subjects of the same sex who were used as controls (Minnesota Med. **16:**698, 1933). Because the same normal controls were not always available for comparison, however, he has now worked out a new method, as follows.

Normal subjects in perfect health and free from all abnormal symptoms have been filmed, using a series of exposures which differ from one another by that exposure necessary to penetrate 0.5 mm. of aluminum. The exposures are measured by means of an aluminum ladder placed on the cassette. This scale varies in thickness from 2.0 to 5.0 mm. The exposures are therefore equivalent to penetrations of 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, and 5.0 mm. of aluminum, respectively.

When the unknown patient reports for examination, the hand and wrist along with the aluminum scale are filmed. For purposes of interpretation the scale on the unknown film is compared with the scale on the control film so that the two scales match perfectly in density. This records the difference in density of the bones between the control and the patient, thereby giving definite information as to the presence of osteoporosis.

Gardner concludes that in the section of Minnesota covered by his report, people who do not use dairy products in the diet very frequently show osteoporosis; this is especially true when the water is "soft," and free from calcium, or when so-called "alkali water" containing excess magnesium is used.

The second part of this study is a statistical analysis of 207 consecutive cases which were studied as described above—58 in males and 149 in females. Females showed greater tendency toward increasing osteoporosis with advancing age than did males, though this difference was not considered great enough to constitute a confusing factor. There appeared to be a lower incidence of osteoporosis among manual workers; osteoporosis seems more a disorder of "white-collar" workers. No relationship could be discovered between gastric acidity and osteoporosis; previous pregnancies seemed to constitute no appreciable factor. There was a relationship between dental decay and osteoporosis. The "best" group was that with adequate calcium intake and normal bowel function; the "worst" group, that with deficient calcium intake and intestinal hypermotility.

The authors conclude with the statement that their study shows a definite positive correlation between osteoporosis and age, condition of the teeth, calcium intake, and intestinal hypermotility; no correlation was found between osteoporosis and sex, civil state, gastric acidity, or pregnancy. PERCY J. DELANO, M.D.

Melorheostosis: Report on a Case with a Review of the Literature. E. L. Franklin and I. Matheson. Brit. J. Radiol. **15:** 185–191, July 1942.

Melorheostosis is a rare bone disease characterized by hyperostosis of one aspect of the bones of one extremity. It is slightly more common in males. The etiology is unknown. The symptoms are vague, usually consisting of pain in the involved limb. The diagnosis rests upon the roentgenological appearance.

The x-ray appearance is that of increased density of one aspect of the bone, usually encroaching upon the marrow cavity more than the periosteal side of the bone. The thickening may resemble osteoma, but usually presents a melted wax-like appearance. There may be cal-

careous deposits in the soft tissues adjacent to the joints.

A case of this disease in a woman of forty-one is reported in detail. In this case there was involvement of almost all the bones on the right side of the body.

SYDNEY J. HAWLEY, M.D.

Diagnosis of Intervertebral Disc Prolapse and Related States. W. Bärtschi-Rochaix. Schweiz. med. Wchnschr. **72:** 729–736, July 4, 1942.

Since intervertebral disc protrusion leads to no symptoms absolutely pathognomonic, a synopsis of the findings on history, neurological examination, orthopedic examination, and roentgen examination is correlated for this condition and allied states. The evaluation of these facts is summarized in a table, as follows:

OF UNCERTAIN VALUE

History

Sciatica
Lumbago
Damage to sphincters or potency
Pain on motion
Pain on sitting or rising
Pain on load
Relief of pain by rest
Recurrence of pain on reactivation

Neurologic examination

Lasègue and Bragard +
Sciatic trigger point
Radicular hyperesthesia
Spasm of lumbar muscles
Damaged tendon reflexes
Damaged sphincter control

Orthopedic symptoms

Sensitiveness of spinous processes to percussion or pressure
Rigidity of lumbar gutter
Absence of lumbar lordosis
Lumbar kyphosis or scoliosis
Pain on forward bending
Pain on rotation
Reversed Lasègue sign

Roentgen signs

Thinned intervertebral disc
Anteroposterior dislocation

OF SUGGESTIVE VALUE

History

Trauma to back, direct or indirect
Protracted physiotherapy valueless
Intermittency
Lumbago plus sciatica
Paresthesia or pain in the calf, in the back of the thigh, in the lumbosacral joint
Pain on coughing or sneezing
Pain in limbs on movement of back
Pain in limbs on bending head

Neurologic examination

Atrophies, pareses
Radicular hypesthesias
Xanthochromic spinal fluid
Reversed Queckenstedt +
Limb pain on head and back motion
Limb pain during Queckenstedt test
Unusual pain on lumbar puncture over site

Roentgen signs

Marked disc narrowing on the side of the symptoms
Typical configuration on myeloscopy and myelography in A-P, lateral, and oblique planes

CONCLUSIVE

Roentgen signs, conclusive in 93 per cent (Hampton)

The use of these points in reaching a diagnosis is illustrated by six typical and six atypical cases.

LEWIS G. JACOBS, M.D.

Persistent Olecranon Epiphyses in Adults. D. H. O'Donoghue and L. S. Sell. J. Bone & Joint Surg. **24:** 677–680, July 1942.

Persistence of the olecranon epiphysis into the adult state is uncommon and previously unrecorded in the American literature. It must be differentiated from epiphyseal separation and from a true patella cubiti.

This report deals with a 31-year-old patient who had injured the right elbow. In the course of the x-ray studies an open epiphyseal plate was found, and studies of the opposite arm showed persistence of the epiphyseal line at the olecranon. The injured elbow was opened and the separated surfaces shown to be covered with cartilage. Apposition was obtained and position held by a screw. Good function resulted.

Reproductions of roentgenograms of both elbows are presented showing the anomaly.

JOHN B. MCANENY, M.D.

Anterior Dislocation of the Distal Extremity of the Ulna; Report of a Case. F. J. Cox. Surgery **12:** 41–45, July 1942.

Anterior dislocation of the distal extremity of the ulna is a rare lesion. A report of one case is given.

A colored female, aged thirty-seven, was riding in a car which turned over. The car came down on the flexor surface of the forearm, which was strained and twisted in disengagement; there were immediate pain and swelling of the wrist and it was impossible to use it without increasing the local pain. Roentgen studies were reported negative, and the patient was sent home. Three weeks later she returned to the hospital complaining of persistent throbbing pain in the right wrist which became worse with any attempt at motion. The pain was referred to the volar aspect of the wrist and local swelling was most marked on the volar surface. Point tenderness was localized over the distal radio-ulnar joint. The original roentgenogram was reviewed and found to show an anterior dislocation of the ulna with a fracture of the styloid process.

An open reduction was done, the distal extremity of the ulna was found lying upon the anterior aspect of the radius and displaced about 1 cm. toward the radial side of the wrist; this displacement was firmly fixed by the contracted pronator quadratus muscle. The capsule having been incised to expose the radio-ulnar joint, a periosteal elevator was inserted as a lever to reduce the dislocation. This could be accomplished only after releasing the origin of the pronator quadratus muscle from the lower inch and a half of ulna. The results were quite satisfactory.

Probably anterior dislocation of the ulna is always associated with either a fracture of the ulnar styloid or a tear of the triangular ligament at its point of insertion into the styloid process. When the patient is seen early, before spasmodic contracture of the pronator quadratus muscle has occurred, reduction of the anterior dislocation of the ulna should be easily accomplished. Where the dislocation has been allowed to remain for a period of time sufficient to permit cellular infiltration and fibrosis within the substance of the pronator quadratus muscle, open reduction becomes necessary.

J. E. WHITELEATHER, M.D.

Gross Pathologic Anatomy of the Unusual Shoulder Specimens in Two Human Cadavers, with Some Remarks Relative to the Surgical Significance of These Findings. T. Horwitz. Surgery **12:** 46–63, July 1942.

(*1*) *Unreduced Anterior Subclavicular Dislocation of the Head of the Humerus of Two Years' Duration:* A specimen was obtained from the cadaver of a white female, aged 69 years, whose death had been due to a malignant lesion of the large intestine with metastases. Two years prior to her death, she had sustained a traumatic dislocation of the right shoulder joint that had remained uncorrected after several attempts at closed reduction had failed. The shoulder could be abducted, internally and externally rotated, and extended 45 degrees. Most of the muscles were well developed and in normal arrangement except for the combined tendons of the supraspinatus, infraspinatus, and teres minor muscles (the musculotendinous cuff), which overlay and terminated in the soft tissues filling the old glenoid cavity, having become completely detached from the greater tubercle. The axillary vessels and brachial nerve plexus were deflected medialward and were angulated over the medial aspect of the humeral head. These structures were not visibly flattened or compressed and appeared normal. The dislocated humeral head lay in a position anterior to the scapula, medial to the coracoid process, and beneath the middle third of the clavicle. The head of the humerus was covered by a thick capsule which was inseparable from the overlying muscles. The new joint cavity was completely closed and had no connection with the glenoid cavity. The humeral head was about two-thirds covered with thin, irregular, degenerated cartilage; the other third was completely denuded. The head was considerably flattened in its posterolateral portion, and this region of the head articulated with a depressed area on the anterior surface of the scapular neck. There were no tendinous attachments to the greater tubercle.

The glenoid cavity was shallow and diminished in its antero-posterior dimensions; the anterior lip was fractured and displaced; the cavity itself was filled with soft tissue and the terminal portion of the musculotendinous cuff.

Specimens of anterior dislocation of the humeral head have been described before. The features stressed by others and demonstrated in the case here recorded are the flattened posterior portion of the enlarged head which articulates with the scapula and the inferior surface of the coracoid process; the formation of a new "glenoid fossa" on the anterior surface of the neck of the scapula; the new capsule enveloping the head, that is formed, in part, from the deep surface of the subscapularis muscle, and that is reinforced, posteriorly, by the tendons of the short rotator muscles; the occasional ossified bodies within the tendons of the subscapularis and infraspinatus muscles; the displaced tendon of the long head of the biceps muscle.

(*2*) *Advanced Degenerative Disease of the Shoulder Joint:* Two shoulder specimens obtained from a colored woman who died at the age of 77 from bronchopneumonia are interesting because they represent the most advanced stage of the degenerative processes that may involve the articulation. The character of the lesions indicates that function may be preserved in the presence of advanced degenerative joint disease, and the ossified plaques in the deltoid muscle, bilaterally, which served as part of the receptive articular surface for the humeral head, represent bony metaplasia in the muscle.

The humeral head, which had eroded completely through the superior portion of the musculotendinous cuff, articulated not only with the glenoid fossa but also with broad facets, formed by considerable bony proliferation, on the deep surface of the acromial end of the clavicle and on the deep surface of the acromion process, as well as with a bony plaque within the substance of the thinned deltoid muscle at its origin. These four bony surfaces presented a smooth, continuous articular surface for the reception of the humeral head. The cartilage of the glenoid cavity was fibrillated and thinned and was absent in the center of the fossa, with exposure of the underlying bone. The glenoidal labrum was absent and replaced by marginal bony proliferation, especially anteriorly and posteriorly. The outer half of the humeral head was flat; there was considerable bony proliferation along the articular margin of the humeral head.

The synovia was thickened and villus and nodule formations were present. The closely surrounding muscles were thin, frayed, and flattened. There were various ossified plaques, formed by metaplasia in the deltoid muscle, which contributed to the formation of a receptive articular surface for the degenerated humeral head. The shadow of these areas of ossification could be misinterpreted, roentgenographically, for calcifications within the musculotendinous cuff or paratendinous soft tissues of the shoulder region.

J. E. WHITELEATHER, M.D.

Adamantinoma of the Tibia: Report of Two New Cases. M. B. Dockerty and H. W. Meyerding. J. A. M. A. **119:** 932–937, July 18, 1942.

Adamantinomas arise from cells which under certain circumstances lay down enamel but which may or may not do so. Enamel has not been found in the tibial tumors which have been reported. The authors believe that these neoplasms arise from squamous cells which have dedifferentiated into modified ameloblasts. The prodigious capacity of cells to dedifferentiate is seen in the many examples of epidermoid carcinomas occurring in sites like the lung and gallbladder, where squamous epithelium does not normally exist.

The part played by trauma in the production of these tumors is difficult to evaluate. The anatomic location would favor a traumatic causation. Whether injuries to the tibia "implant" epithelial cells into the periosteum of the underlying bone and, if they do so, what type of "thwarted repair" (Ryrie: Brit. M. J. **2:** 1000, 1932) process might give rise to tibial adamantinomas are matters which still are lacking in actual demonstration. It is interesting, however, that where nature pro-

vides such a possibility, *par excellence*, these tumors make their appearance to the exclusion of other situations.

Of particular interest in one of the authors' cases was the unusual and unexpected extent of the tumor. This observation has been made by others and undoubtedly accounts for the high "recurrence" rates observed following even such semiradical operative procedures as excision with bone grafting. In both the authors' cases the disease had existed over a long period. Trauma appeared a probable etiologic factor in one case and a possible factor in the other. In one case the lesion was so extensive as to require amputation. The microscopic picture of this case is recorded in detail because in its variability of cellular architecture it afforded connecting links between the seemingly different "varieties" of adamantinoma recorded in the literature.

The same degree of osteitis fibrosa present in both cases is of unusual interest. Just why this localized bony rarefaction should occur is not known. It may have been due to a nutritional change resulting from circulatory obstruction by the tumor.

Fifteen cases of adamantinoma of the tibia have previously been reported in the literature.

CLARENCE E. WEAVER, M.D.

Development of Sarcoma in Myositis Ossificans: Report of Three Cases. G. T. Pack, and R. R. Braund. J. A. M. A. **119:** 776–779, July 4, 1942.

Myositis ossificans has been described as a deposition of bone in muscles or about their insertions and as a low-grade inflammatory process characterized by the formation of bone within or in contact with muscle. The lesion involves primarily the fascial connective tissue, any muscular changes being secondary and degenerative. The lesion may occur as myositis ossificans conscripta, due to repeated slight injuries or irritations in multiple or single areas. A localized form may occur in a single muscle without any history of trauma or other causative factor. Myositis ossificans progressiva usually begins in the muscles along the spine and gradually spreads until it involves all the muscles of the body.

It is generally agreed that the plates of bone in these lesions arise from the connective tissue through an intermediary cartilaginous stage. Muscles about the elbow joint and the adductors of the thigh are the most frequently involved. Barr believes that myositis ossificans progressiva results from a true metaplasia of connective tissue to bone. In this form of the disease there are associated defective anatomic and physiologic formations, mostly involving the fingers and toes.

Shipley (Arch. Surg. **41:** 516, 1940) found 4 cases recorded of the development of osteogenic sarcoma in pre-existing myositis ossificans traumatica. To these the authors add 2 cases in which osteogenic sarcoma developed in pre-existing myositis ossificans circumscripta and a third case in which myositis ossificans progressiva was associated with a sarcoma developing in the muscles of the back.

Two of these patients had myositis ossificans in the upper portion of the thigh. One had a history of injury, the other did not. One died with metastases in the lungs, the other with metastases in the lungs and cerebrum. Both received high-voltage roentgen and radium therapy. Both were male adults, aged thirty-six years and twenty-seven years, respectively. The third patient was a boy aged seven years, with typical physical and roentgen findings of myositis ossificans progressiva. A malignant tumor infiltrating the right trapezius and rhomboid muscles was present. A biopsy was taken and reported as malignant tumor, probably myxoliposarcoma. Complete regression of the tumor and enlarged lymph nodes in the neck followed two courses of high-voltage roentgen therapy.

The three case histories are given in detail and there are numerous illustrations and roentgenograms illustrating the clinical and pathologic features of the disease in these interesting cases.

CLARENCE E. WEAVER, M.D.

Diagnosis of Multiple Myeloma by Sternal Aspiration. L. H. Beizer, B. E. Hall, and H. Z. Giffin. Am. J. M. Sc. **203:** 829–836, June 1942.

According to Ewing the term myeloma designates tumors of the specific bone marrow cells, including the lymphocyte, granular leukocyte, and the red cell series; it is not applicable to tumors arising from fat tissue or blood vessels or to those derived from indifferent endothelial cells. Four types of myeloma have been reported; the plasma-cell type, the myelocytoma, the lymphocytoma, and the erythroblastoma. These differ only in the cytologic composition of the tumor and not in the gross appearance or the clinical course.

The identification of the cell type depended for many years on histologic sections. Since the advent of sternal aspiration, the cells have been classified according to their appearance in stained dry smear preparations. Although most of the tumors studied in this way have been classified as of the plasma-cell type, the matter has been complicated by the fact that criteria for the recognition of the typical plasma cell vary widely. Nor is there any agreement on the origin of these cells.

The manifestations of the disease often focus attention away from the underlying cause rather than toward it. Geschickter and Copeland gave six cardinal clinical signs of multiple myeloma, two or more of which are usually present. These are (1) multiple involvement of the skeletal trunk in an adult, (2) pathologic fracture of a rib, (3) the excretion of Bence-Jones bodies, (4) characteristic backache with signs of early paraplegia, (5) anemia, and (6) chronic nephritis with nitrogen retention, low blood pressure, and high serum proteins. Other important features which are often noted are (1) hyperproteinemia with reversal of the albumin-globulin ratio, (2) hypercalcemia with normal or high serum phosphorus, (3) evidence of autohemagglutination in the counting chamber, on blood smears, or in the small vessels of the fundus, in which the blood has a cayenne pepper appearance when seen through the ophthalmoscope while pressure is being placed on the eyeball; (4) the occurrence of an anticomplementary reaction when a complement-fixation test is carried out.

The conditions with which multiple myeloma is most often confused are metastatic skeletal lesions, hyperparathyroidism, spondylitis, nephritis, and leukopenic leukemia. While biopsy is often undesirable, sternal aspiration, because of its simplicity, is rarely contraindicated. Without its use a definite diagnosis is often impossible during the life of the patient.

Ten cases of multiple myeloma were studied within a period of two years. In each the examination of the sternal marrow was done because the condition

was in some way atypical. Only one patient did not have anemia. Autohemagglutination was present in 7 cases, a leukemoid reaction was found in 4, and in 2 myeloma cells were seen in the peripheral blood. In 6 of the 7 cases in which the total serum proteins were determined a hyperproteinemia was found; in these cases the albumin-globulin ratio was reversed. Bence-Jones proteins were present in the urine in 6 cases. The sedimentation rate was elevated in all.

In 7 of the 10 patients roentgenologic changes were recognized, but in only 2 were they considered as typical. In one case generalized osteoporosis and pathologic fracture of one vertebra were found. In 4 cases it was impossible for the roentgenologist to distinguish definitely between multiple myeloma and metastasis.

A modification of the Arinkin method was used in performing sternal aspirations. Smears were made and stained with Wright's stain followed by Giemsa's stain.

Plasma cells, morphologically identical with those seen in the peripheral blood, make up less than 1 per cent of the leukocytes obtained from normal persons; an increase is suggestive of multiple myeloma. The most characteristic and readily recognizable of the cells encountered were those with an abundant, definitely outlined, deeply basophilic cytoplasm, a round, eccentrically placed nucleus of moderate size, having a fairly coarse chromatin sharply demarcated from the parachromatin, and a very large nucleolus. These cells, having a large nucleolus, designated myeloma cells, were present in 8 cases. They were not found in any other condition and were considered pathognomonic. Variations from this description, involving all parts of the cell, were noted from case to case, or even in the same case. In one case, the characteristic myeloma cells were not found, nor were the plasma cells increased in number. This indicates that the sternal marrow had not become involved, and that the absence of abnormal findings does not necessarily exclude the diagnosis.

BENJAMIN COPLEMAN

Eosinophilic Granuloma and Certain Other Reticulo-Endothelial Hyperplasias of Bone: Comparison of Clinical, Radiologic, and Pathologic Features. P. Gross and H. W. Jacox. Am. J. M. Sc. **203:** 673–687, May 1942.

The authors believe that eosinophilic granuloma of bone is identical with Hand-Christian disease and related to the other reticulo-endothelial hyperplasias of bone such as Letterer-Siwe's disease (non-lipoid reticulo-endotheliosis).

The histologic descriptions of eosinophilic granuloma in the various reports have been uniform with the exception of minor details, such as the degree of phagocytic activity shown by the stromal cells and the presence or absence of multinucleated giant cells, mitotic figures, and areas of necrosis, scarring, or new bone formation. The explanation for these discrepancies may lie in the fact that the biopsies represent different stages of the granulomatous process. The histologic picture regarded as characteristic of eosinophilic granuloma of bone is also found in Hand-Christian disease. Both conditions show destruction and replacement of normal tissues by granulomatous tissue in which endothelial cells predominate. The latter may contain lipoid. In 9 of the 84 cases of Hand-Christian disease lipoid-containing cells were not found in the biopsy or autopsy material. Eosinophilia has been noted in both Hand-Christian disease and in eosinophilic granuloma. The presence of hypercholesterolemia has not been determined in eosinophilic granuloma, but has been, at times, associated with Hand-Christian disease. Because all of the cases have been cured, it has not been possible to determine if visceral changes occur in eosinophilic granuloma. However, reports of eosinophilia in a draining lymph node, in sternal marrow, and in the peripheral blood indicate that, in addition to the solitary bone lesion, there may be widespread and even systemic changes.

The radiologic appearance of the bone defects in eosinophilic granuloma and Hand-Christian disease is similar except for the multiplicity in the latter. In either condition, the lesions may heal spontaneously or following irradiation. While there is no mortality in eosinophilic granuloma, there is a 30 per cent mortality in Hand-Christian disease.

Letterer-Siwe's disease is a non-lipoid reticulo-endotheliosis which affects infants and children predominantly, and is nearly always fatal. The lesions are identical with those of Hand-Christian disease radiographically; histologically, they are usually devoid of lipoid, but cases have been reported where small amounts of lipoid were present. Biopsies from lesions of Hand-Christian disease may show little or no lipoid.

Histologically and radiographically, there may be little to differentiate a solitary xanthoma of bone from eosinophilic granuloma or the individual lesions of Hand-Christian disease or Letterer-Siwe disease.

Our knowledge of the diseases involving the reticulo-endothelial proliferations, focal or general, is far from complete. There does not appear to be any distinctive pathologic or radiographic feature to justify their segregation into separate disease entities. The existence of cases with features intermediate between Hand-Christian disease and Letterer-Siwe disease suggests that a sharp distinction between these conditions may not be valid. [A similar view is expressed by Green and Farber: J. Bone & Joint Surg. **24:**499, 1942. Abst. in Radiology **40:**107, January 1943.]

BENJAMIN COPLEMAN

Mixed Tumors of the Spinal Canal. L. A. French and W. T. Peyton. Arch. Neurol. & Psychiat. **47:** 737–751, May 1942.

The authors classify mixed tumors into three types: teratomas, which are composed of organs representing all three germ layers; dermoids, which contain mesodermal and epithelial tissues; epidermoids, which contain tissues of epithelial origin but lack definite dermal structures. Three examples of mixed tumors of the spinal canal, presented in detail, form the basis of this article; two were teratomas while one was an epidermoid cyst.

The roentgen appearance of mixed tumors of the spinal canal is characteristic. While pressure erosion may occur with any benign intraspinal tumor, mixed tumors are characterized by a diffuse fusiform enlargement of the spinal canal extending over several vertebral levels. These tumors cause erosion of the posterior surfaces of the bodies of the vertebrae, thinning of the laminae, and narrowing of the pedicles, with resultant increase of the interpedicular distances. Because no normal range for the interpedicular distances

in children had been determined, the authors measured these distances for the lower thoracic and lumbar spine in 100 subjects up to ten years of age, and present their findings graphically. In order to determine whether a spinal canal is enlarged, its measurements must be compared with the normal range in the patient's age group. A canal that is larger than normal or in which the interpedicular distances are increased 2 to 4 mm. in consecutive vertebrae shows evidence consistent with a diagnosis of mixed tumor.

The paper is well illustrated and has a good bibliography. CORNELIUS G. DYKE, M.D.

Hyperparathyroidism with Metastatic Deposits in the Kidneys. A. A. Werner. South. M. J. **35:** 671–676, July 1942.

Parathormone, which is quantitatively increased in hyperparathyroidism, serves to mobilize calcium from the bones, producing the typical osseous changes seen in osteitis fibrosa cystica. Many cases of this condition show deposits of calcium in various tissues and organs in the body. Renal calculi are not uncommon.

A case is reported here of a 62-year-old female with symptoms of urinary frequency, pain, and burning of two years' duration. Urological study demonstrated a large right renal concretion, which was removed. The patient returned five years later with a recurrence of her old symptoms. Large bilateral renal concretions were found. Roentgenograms of the skeleton showed diffuse decalcification of spine, pelvis, long bones, and skull, though the characteristic cysts of osteitis fibrosa cysticum were not made out. Autopsy revealed a tumor 4 × 2 cm. lodged behind the thyroid, proved histologically to be a parathyroid adenoma. Bibliography and illustrations are included.

MAX MASS, M.D.

RADIOTHERAPY

MALIGNANT TUMORS

Carcinoma of the Skin. R. L. Sutton, Jr. J. Missouri M. A. **39:** 203–207, July 1942.

Of a series of 1,500 specimens of tumors of the skin which were subjected to histologic scrutiny and statistical analysis, 560 were found to be basal-cell carcinomas. Of these, 82 per cent occurred on the face, while the head and neck together were the site of 95.6 per cent. There was no sex predilection for this tumor. None occurred on the feet, digits, or genitals, or in the oral mucosal regions. Three-quarters of all lesions removed from the eyelids and upper lip were basal-cell carcinomas. An apparently significantly higher proportion of all lesions from the temple, ear, and hand were basal-cell carcinomas in males than in females, and an apparently significantly higher proportion of all lesions from the forehead, upper lip, and trunk and extremities were basal-cell carcinomas in females than in males. Tables are included showing the histologic diagnosis of the 1,500 cutaneous lesions which were clinically thought to be neoplastic, and basal-cell carcinomas are further analyzed according to location, sex distribution, and sites of predilection.

L. W. PAUL, M.D.

Primary Carcinoma of the Lung. (Report of 115 Cases, 38 Autopsies and 77 Bronchoscopic Biopsies.) J. A. Perrone and J. P. Levinson. Ann. Int. Med. **17:** 12–25, July 1942.

Rosahn (Am. J. M. Sc. **179:** 803, 1930) is quoted to the effect that definite criteria for diagnosis should be established to render valid any comparisons of the incidence of carcinoma of the lung at different periods. These criteria are as follows. (1) An autopsy must have been performed. (2) The carcinomatous nature of the lesion must have been verified microscopically. (3) There must be no reasonable doubt that the neoplasm was a primary growth. (4) Percentage should be calculated on the basis of total adult necropsies. Rosahn arbitrarily adopts twenty years as the lower age limit.

The authors present a series of 115 primary carcinomas of the lung, of which 38 came to autopsy. Seventy-seven were diagnosed by means of a bronchoscopic biopsy. The following conclusions are reached: (*a*) There has been a relative and absolute increase in incidence. In the authors' series primary lung cancer accounted for 13 per cent of the total number of carcinomas. (*b*) Cough, dyspnea, hemoptysis, and pain are four cardinal symptoms of carcinoma of the lung. (*c*) Bronchoscopic examination is by far the most important diagnostic procedure available and should be done in all cases of persistent cough, whether dry or productive. (*d*) Of 77 cases diagnosed by bronchoscopic examination, only 3 were amenable to surgical treatment. (*e*) Of 77 patients, 76 were dead within three to eighteen months from the time the diagnosis was made. (*f*) Lobectomy or pneumonectomy in suitable cases is the treatment of choice.

In regard to the irradiation treatment of primary carcinoma of the lung, the authors reported a limited number of patients in this series to have been treated by such methods. The technical factors are not described. No apparent benefit was obtained from deep roentgen therapy. In addition it tended to produce inflammatory reactions and to result in many systemic reactions, such as loss of appetite, nausea, and vomiting.

J. A. L. MCCULLOUGH, M.D.

BENIGN CONDITIONS

How Shall We Treat Fibroids of the Uterus? Wm. H. Vogt. J. Missouri M. A. **39:** 207–209, July 1942.

Modern treatment of fibroids of the uterus may be expectant, surgical, or radiologic. Expectant treatment is limited to those tumors which are symptomless, small in size, and so located as not to produce difficulty if operation later becomes necessary. The age of the patient also is important, since after the late thirties, small fibroids, even when multiple, do not in the majority of instances increase to any dangerous size. During the twenties and early thirties, these tumors usually do grow and are apt to attain large proportions which may require hysterectomy. In young women, therefore, it is advisable to remove small tumors by myomectomy even when they are producing no symptoms. The author believes that the large symptomless fibroids should always be treated surgically except when serious constitutional complications make surgical intervention too dangerous. The medical

treatment of fibroids can be dismissed with the statement that it is of no value other than for the purpose of putting the patient in the best possible condition for a future operation. After the menopause, hysterectomy is the operation of choice except for pedunculated submucous tumors, which should be removed by vaginal myomectomy on account of the danger of peritonitis from *S.reptococcus* infection. In the child-bearing age, myomectomy is the most satisfactory procedure if the case is properly selected. Hysterectomy in young women should never be done unless absolutely unavoidable. Abdominal operations are preferred for most patients, and by most operators, because they can be performed with better visualization. In the hands of experienced operators, however, vaginal hysterectomy may involve even less risk than the abdominal operation.

The chief indication for the use of radium is the alleviation of bleeding, but not necessarily the disappearance of the tumor. One of the chief disadvantages of radiation treatment is that the rays are not specific for or limited to the new growth and the function of the ovaries is definitely disturbed. Therefore, it should not be used in young women. Radium is contraindicated when the tumor is large, 12 cm. or more in diameter, or when it is pedunculated or submucous. It must not be used in rapidly growing tumors or those which are undergoing degeneration. The presence of infection in the pelvis, the existence of an accompanying pregnancy, the presence of other tumors, and pressure symptoms, all are contraindications to its use. A curettage should always be done first to determine the possible existence of a malignant lesion. The author prefers the intrauterine application of radium to external application of roentgen rays.

L. W. PAUL, M.D.

Radium Therapy for Vulvar Condylomas. S. L. Wolters and H. Close Hesseltine. J. A. M. A. **119:** 874–877, July 11, 1942.

Until recently condyloma accuminatum or venereum was looked upon as probable evidence of a present or prior gonorrheal infection; hence the lay name "venereal warts." It is now acknowledged that any chronic persistent vulvovaginal discharge (venereal or non-venereal) may precede or be concomitant with these "warts."

Surgical excision may be associated with excessive and even serious loss of blood. Recurrences are frequent after surgical removal. Treatment with keratolytic agents is hazardous and unpredictable in its results. Schmitz records a series of 13 cases in which roentgen therapy was used, with recoveries in 11. It should be borne in mind that condylomas which develop during pregnancy at times vanish spontaneously after parturition.

In a series of 11 cases, 6 obstetric and 5 gynecologic, the authors used the topical application of radium as the sole means of treatment. The radium used was in two capsules of 50 mg. each and was contained in 0.5 mm. platinum capsules and filtered through 1 mm. of aluminum. The radium in its container was placed directly over the portions of the vulva affected and held in place with strips of adhesive and a perineal pad. When necessary, the radium was moved from one site to another for the estimated dose. Repeated applications were made in those instances in which the first treatment was insufficient. In one instance in which the lesions were confined to a small area, only 75 mg.-hr. of radium were necessary. In another case with extensive involvement 450 mg.-hr. had to be used. This was divided into two applications one month apart. The optimal dose seems to be about 100 mg.-hr. to an area of about 4 sq. cm.

The retrogression or disappearance of the lesions should occur gradually and within a few weeks at most; if not, more radiation is indicated. The response is more directly related to the extent of the lesions than to the age of the condylomas. The method is simple and can be carried out in the physician's office in any community where radium is available.

CLARENCE E. WEAVER, M.D.

Suppurative Parotitis. N. A. McCormick. Canad. M. A. J. **47:** 29–33, July 1942.

Parotitis is a serious complication of surgery and requires immediate treatment. Rankin and Palmer in 1930 showed that immediate use of radium over the infected gland materially reduced the incidence of suppuration (Ann. Surg. **92:** 1007, 1930). A large dose was not necessarily more effective than a medium-sized one. They gave a maximum of four treatments, at eight-hour intervals and of eight hours' duration: 200 mg. radium, 1 mm. platinum filter, at 2.5 cm. skin distance. The maximum dose was 6,605 mg.-hr. The minimum dosage was two applications each of 50 mg. for eight hours at eight-hour intervals, totaling 800 mg.-hr. There was no change in the first twenty-four to forty-eight hours following treatment, but after this the infection rapidly subsided.

F. M. Hodges (Am. J. Roentgenol. **35:** 145, 1936) wrote that most acute, subacute, and chronic cases responded well to from three to five doses of 125 r, at 125 kv., filtered by 4 to 6 mm. of aluminum.

The series of 20 cases here reported was begun in 1937. The treatment is considered as an emergency measure. The involved area is given 150 to 200 r measured in air, at 200 kv., 50 cm. skin target distance, and 0.5 mm. of copper and 3 mm. of aluminum filtration, or 1 mm. of copper and 4 mm. of aluminum, usually over an area 10 × 15 cm. If bilateral involvement is present, both sides are treated. If treated first in the morning, the patient is usually given a similar exposure late in the afternoon and 150 to 200 r each succeeding day until adequate improvement results. Cases seen sixteen or more hours after onset should also be treated, as they may subside satisfactorily.

Surgical intervention should be delayed and, if necessary, should consist only of very simple incisions. Irradiation results in marked reduction of the morbidity and high mortality of this disease.

M. L. CONNELLY, M.D.

Blood Cholesterol as an Indicator of the Therapeutic Response of Patients with Hyperthyroidism. A. Beutel. Strahlentherapie **69:** 400–406, 1941.

The author studied the cholesterol content of the blood in 50 patients with hyperthyroidism undergoing radiation therapy. He found that those whose blood cholesterol content was below normal responded quickly to radiation therapy. The cholesterol content increased rapidly, first exceeding and then slowly returning to normal. Those who had a high blood cholesterol before treatment responded more slowly.

ERNST A. POHLE, M.D., PH.D.

RADIATION REACTIONS

Physical Diagnosis of Radium Poisoning. B. Rajewsky. Strahlentherapie **69:** 438–502, 1941.

The author briefly outlines the problems which are involved in the determination of radium deposits in the body of both the living and dead human being and describes in detail the measuring instruments and methods used in his institution. The determination of the radium emanation content of the expired air and of the urine and the feces, as well as of the radium content of the blood, is included. The various methods based on gamma-ray measurements are described, as is the estimation of the radium content of tissues by means of the emanation method and by the Geiger counter. Finally the author outlines rules which should be followed in order to prevent radium poisoning.

ERNST A. POHLE, M.D., PH.D.

Cardiovascular System of American Roentgenologists Beyond the Age of Forty-five Years. W. Raab. Am. J. Roentgenol. **47:** 555–562, April 1942.

Questionnaires were sent to 737 roentgenologists of the United States and Canada over the age of forty-five, and 344 of these were returned with answers. The questions concerned blood pressure, presence of albumin in the urine, evidence of peripheral arteriosclerosis, and cardiac symptoms, particularly those of coronary disease. The blood pressure level is the only one of these conditions which can be compared statistically with a large group of normals. The average blood pressure levels of the 344 roentgenologists were slightly lower than the accepted normal in all age groups up to the sixty-fourth year, and considerably lower in the age ranges from sixty-five to seventy-four years. This agrees with the observations of Pfahler in 1921.

Peripheral vascular disease and severe nephrosclerosis appeared to be relatively uncommon, although the data did not permit statistical evaluation. The incidence of coronary disease, both without and with thrombosis, was found to be high. The majority of these cases were in heavy smokers (63 per cent of the angina cases and 62 per cent of the thrombosis cases), and the author considers this a possible factor which may have superseded any irradiation effects on the coronary arteries. Of the 344 roentgenologists, 29 per cent were moderate and 38 per cent heavy smokers.

The reason for the low blood pressure levels in roentgenologists and the relatively low incidence of peripheral vascular disease is uncertain because of a variety of complicating factors. The hypothesis is advanced that "prolonged exposure of the entire body to minute roentgen doses may exert a certain protective effect against an exhausting and ultimately destructive overactivity of the suprarenal hormones and related substances within the myocardial and arterial muscular tissues."

H. H. WRIGHT, M.D.

Management of X-Ray Reactions. N. S. Finzi. Brit. J. Radiol. **15:** 192–193, July 1942.

Reactions following 1,000 kv. irradiation are sharper and drier and subside more quickly than those following 200 kv. irradiation. For the same biological effect upon the skin, more roentgens are required at the higher voltage, in the ratio of three to two.

The *erythema* reaction is less severe when the skin is kept dry. Starch powder, calamine, zinc stearate, magnesium silicate, or combinations of these powders are satisfactory for this purpose.

For *vesication* a calamine liniment with two grains of phenol per ounce is a good application. In very painful cases 5 per cent benzocaine may be added.

Acute ulceration may be treated by the application of 5 per cent benzocaine in vaseline. The sulfonamides are sometimes useful.

For *chronic ulceration* the application of the sulfonamides, sulfathiazole, or flavine in paraffine or castor oil is satisfactory. Excision of the ulcer and grafting may be necessary. Ultraviolet light has been found unsatisfactory.

Mucous membrane reactions occur earlier than skin reactions and subside more rapidly. Linseed tea or potassium chlorate lozenges may be helpful. Carbonated water may be more effective than plain water in dryness of the mouth and throat.

For *diarrhea*, salol in 10-grain doses with meals may be helpful. It may be necessary to give some preparation of opium, as Dover's powder or paregoric. No satisfactory method of treatment for *tenesmus* has been found, except narcotics.

Conjunctivitis may be treated by irrigations with 2 per cent salt solution and the instillation of castor oil. *Corneal ulceration* due to irradiation is best treated by sewing the lids closed.

As the lungs are quite sensitive, *pulmonary injury* should be avoided by using tangential irradiation where possible. Respiratory infections should be avoided.

Operation in previously heavily irradiated tissues should be advised with caution, as there is a certain amount of tissue devitalization.

Nausea and *vomiting* may yield to 10-minim doses of adrenalin every hour, also chloretone in 15-grain doses. Nembutal may be useful. Large doses of vitamin C have been advised. Liver extract has not proved successful.

SYDNEY J. HAWLEY, M.D.

Treatment of Ulcers and Third Degree Reactions Following Radiation Therapy and Other Slowly Healing Wounds. H. Auler, W. Schilling, and C. Woite. Strahlentherapie **69:** 417–422, 1941.

The authors describe their method of treating late reactions and ulcers following irradiation. They first rinse the wound with rivanol-sodium chloride solution and then apply a dressing soaked in sodium chloride solution, which is left in place for several hours. The dressing is then removed, plasma is applied by means of a pipette to the ulcerated surface, and the wound is left exposed until coagulation has occurred. The surrounding tissue may be covered with cod-liver-oil ointment. The wound is then dressed again with gauze soaked in sodium chloride solution. This treatment may be repeated daily until the wound is clean. A dressing is then applied which contains some stimulating substance. The authors have had excellent results with this procedure and append several illustrative case histories.

ERNST A. POHLE, M.D., PH.D.

THE BETATRON

A Twenty Million Electron-Volt Betatron or Induction Accelerator. D. W. Kerst. Rev. Scientific Instruments **13:** 387–394, September 1942.

The induction accelerator is a machine for whirling negative electrons between magnets somewhat as the well known cyclotron whirls positive ions. It is to be looked upon as a transformer in which the high-tension secondary current, instead of being constrained to run in a circular path around the magnetic core in an insulated wire, is held to travel in a circular path because it consists of bare negative electrons moving in a strong magnetic field.

The twenty million electron-volt betatron described here has actually been built and put in operation at the University of Illinois. The magnet weighs approximately $3^1/_2$ tons and has to be made of laminated transformer steel, because it is actuated by an alternating current, at 180 cycles per second. The pole pieces are 19 inches in diameter and between lies the vacuum chamber, which is 2 inches thick. Into this vacuum vessel projects an injector for the negative electrons which is something like an x-ray tube with a ring anode so that the cathode rays shoot right out the back of it tangentially to the circular orbit that the electrons subsequently follow in the big vacuum chamber. The accelerating voltage is about 20 kilovolts. The injection is made during a period of a few microseconds at the beginning of the alternating current wave in the big magnet. Because these electrons are moving in the magnetic field, they are constrained to run in a circle. Because the magnetic field is on the increase, they are accelerated by the induced electromotive force just as the current is made to flow in the windings of an ordinary transformer. As they get to going faster, they would naturally fly out into orbits of larger diameter, excepting only that during the same time the magnetism of the big magnet is increasing, which again pinches them down into a smaller orbit. By careful shaping of the pole pieces, it is possible to make things come to equilibrium so that the negative electrons travel in a very narrow, well defined orbit. The electrons reach their maximum speed at the end of the first quarter cycle, by which time they have traveled a total path of some 800 kilometers. Relativity, which interferes with the nicely timed acceleration of the ions in the conventional cyclotron when the speeds approach the speed of light, as happens in electron acceleration, interferes not at all with this accelerator because the curvature of the path depends on the momentum of the particle, and it makes no difference what portion of the momentum is assigned to mass and what portion to speed.

Just before the end of the first quarter cycle, a heavy reverse current is shot around the magnet from a condenser, which quickly reduces the magnetic field in the big magnet, and so lets the whirling electrons fly out into an orbit of larger diameter. As the orbit expands, the electrons begin to run into the back of the electron injector, which is made of heavy tungsten, so that it becomes the target of the x-ray tube.

The x-ray tube current ends up at only about one microampere, but on account of the extremely high voltage, the efficiency is enormously increased so that about 65 per cent of the energy in the cathode beam is actually turned into x-ray energy. The output measured at one meter distance with a Victoreen roentgen meter is 16 r per minute. A large quantity of diffused and transmitted high-speed electrons also escapes from the machine.

The windings of the magnet consist of 81 turns of double cable about each pole. The total cross-section of the double cable is equivalent to a single rod of copper 0.4 inch in diameter. The cables are insulated with 0.005-inch glass tape. When the whole 162 turns are in series, the coil current runs 106 amperes and nearly 17,000 volts at 180 cycles per second. This would be 1,700 kilowatts if it had to be supplied by the power lines. However, the stratagem has been adopted of building the magnet into a tuned circuit with a large condenser bank (5.5 microfarads) so that its natural frequency is 180 cycles per second. The loss in the condenser bank is 6 kilowatts, and the iron losses are 20 kilowatts. This power loss is supplied by a six-turn primary winding around the coil boxes, which is supplied from the 700-volt frequency tripler.

X-rays produced at twenty million volts get into the cosmic ray range, and are capable of producing nuclear disintegrations. The high-speed negative electrons which escape from the machine have ten times the energy of the most penetrating beta rays from radium, and are enormously penetrating in flesh. Their method of absorption in the body differs from that of x-ray in that they run out to a definite range (something on the order of 10 cm. for this energy) and are there absorbed in a comparatively short distance. There is a possibility with these high-speed beta rays, therefore, that one could produce very large depth doses with very small skin doses.

[Two papers on the Betatron appear in this issue of RADIOLOGY, pp. 115 and 120.]

R. R. NEWELL, M.D.

EXPERIMENTAL STUDIES

Studies on the Value of X-Ray Therapy in Experimental Gas Gangrene Infection. E. Singer. M. J. Australia **2:** 1–3, July 4, 1942.

The author has carried out experiments on groups of mice which were infected intramuscularly with *Clostridium welchii* or *Vibrion septique*. In one series x-ray therapy was combined with local applications of sulfanilamide powder. Single doses of radiation of 50 or 100 r were given. When sulfanilamide was used the application consisted of 2.5 mg. The details of the experiment are presented in tabular form.

The author concludes that the x-ray treatment of mice infected intramuscularly with either *Clostridium welchii* or *Vibrion septique* is ineffectual. He believes that the demonstration of *Clostridium welchii* in a wound does not necessarily indicate gas gangrene since

the organism occurs as a normal saprophyte in the intestines, the mucous membranes, and in the skin. He also states that it is unusual for gas gangrene to be due to only one of the anaerobic organisms. He believes that a mixture of pathogenic and apathogenic anaerobes together with aerobes participate in the clinical entity of "gas gangrene" in contrast to experimental infections with pure cultures of high virulence. It is his opinion that wounds containing a mixed flora of low virulence, some of which are gas gangrene organisms, will respond to x-ray therapy, while the pure, highly virulent infections will not yield to such treatment. He regards sulfanilamide and antitoxic serum as the treatment of choice for the virulent type of gas gangrene infection. The serum therapy acts only on the toxemia and does not affect the bacilli, while the sulfanilamide kills or prevents the multiplication of the organisms.

DONALD R. LAING, M.D.

Action of Roentgen Rays on Rat Testicles. H. von Wattenwyl. Schweiz. med. Wchnschr. **72:** 765–766, July 11, 1942.

The work here described was undertaken with the idea of injuring the testicles of rats and studying the influence of various hormones on their regeneration. Control studies of regeneration without hormone administration are reported in this paper. Doses of from 60 to 2,400 r (factors not given) were administered and the testicles were examined four to fifty days later. The findings confirm those previously reported by Regaud and by Schinz and Slotopolsky. The spermatogonia were the most sensitive cells, showing changes after the smallest dose given. The injury to these "mother-cells" (*sic!*) led to a gradual disappearance of the generative cells in the canaliculi. With increasing doses, this change occurred faster, and regeneration was longer delayed. With heavy doses all cells in the seminal epithelium were injured. With doses of 2,400 r the spermatozoa were injured and atypical mitoses and giant cells were seen; interstitial cells remained uninjured even with these large doses. Histologic examination of the epididymis was also made, and this gave an answer to the question of the fate of the damaged epithelium. The epithelium of the epididymis remains undamaged, but the content of the ducts changes from spermatozoa to separated epithelial cells. Such damaged epithelium can also be recovered in the ejaculate. A phase immediately following radiation during which normal spermatozoa are found in the ejaculate, and which becomes shorter the greater the dose, suggests that the damaged epithelium crowds spermatozoa still in the epididymis out into the seminal ducts. Test of this hypothesis by mating the irradiated animals with normal females shows that there is in fact a period of normal fertility, followed by a period of lessened fertility, followed in turn by a period of normal fertility. After 1,800 r, fertility is abolished in four days, although morphologically the ejaculate is normal. The offspring in the second and third generations following radiation have been studied and found normal up to the time of the report.

LEWIS G. JACOBS, M.D.